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PRECLINICAL AND CLINICAL TESTING BY THE PHARMACEUTICAL INDUSTRY, 1980—DMSO

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HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH AND SCIENTIFIC RESEARCH

OF THE

COMMITTEE ON LABOR AND HUMAN RESOURCES UNITED STATES SENATE

NINETY-SIXTH CONGRESS

SECOND SESSION

ON

EXAMINATION OF TESTING OF DMSO AND FDA'S ROLE IN THE PROCESS

JULY 31, 1980

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Committee on Labor and Human Resources

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PRECLINICAL AND CLINICAL TESTING BY THE PHARMACEUTICAL INDUSTRY, 1980—DMSO

THURSDAY, JULY 31, 1980

U.S. SENATE,
SUBCOMMITTEE ON HEALTH AND SCIENTIFIC RESEARCH,
COMMITTEE ON LABOR AND HUMAN RESOURCES,
Washington, D.C.

The subcommittee met, pursuant to notice, at 9:18 a.m., in room 4232, Dirksen Senate Office Building, Senator Edward M. Kennedy (chairman of the subcommittee) presiding.

Present: Senators Kennedy, Metzenbaum, Schweiker, and Hatch.

OPENING STATEMENT OF SENATOR KENNEDY

Senator KENNEDY. We will come to order.

Today, the Senate Health Subcommittee will hear the story of DMSO. It is a sad story, sad because hundreds of thousands of Americans suffering from a variety of painful and often disabling diseases have placed their hopes in this drug, and yet after 18 years we still do not know whether or not those hopes are misplaced. It is a story of failure—failure of the bureaucracy at the Food and Drug Administration to handle the drug appropriately, to expedite a complete and timely review, to detect serious deficiencies in scientific data submitted on the drug's behalf, to satisfy the public that it is doing all it can to develop definitive answers; failure of the private sector to conduct competent and acceptable scientific research on the drug, to adequately monitor the quality of work being done, and to cooperate fully with the FDA investigations of possible wrongdoing. This failure of both Federal and industrial responsibility has had a very high cost: the erosion of public confidence in the ability of government—in this case, the FDA—to work, to respond to human suffering, to meet people's needs.

As a result, over 100,000 Americans use DMSO each year. They get it however they can: in some cases legally, in some cases not; in some cases in forms designed for human use, in some cases not. A tiny minority of these people use DMSO for its one legitimately approved purpose, but in most cases they use it for unapproved purposes. Some rub it on their skin; some drink it; some are treated intravenously. By the tens of thousands, Americans are making individual judgments to try DMSO for arthritis, for ankle sprains, for neurological trauma, and for a variety of other reasons. Others are desperate to try it. And many of those who use it believe that they are helped, and tell their friends, and the use of

the drug spreads. We will hear some of these case histories this morning, and they are impressive.

But it is important to remember that the proper place to evaluate the safety and effectiveness of a new drug is in the Food and Drug Administration, not the news media. The proper way to evaluate it is by scientific, medical trials conducted by the drug company, not by individual subjective judgments. This Nation has always insisted, and rightly so, that a drug be proven safe and effective before it is marketed. This safeguard has spared the Nation the thalidomide-like tragedies. And, yet, a very fine balance must be maintained by the Food and Drug Administration, for as tragic as it may be to let an unsafe drug on the market, it may be equally tragic to keep breakthrough drugs off the market—drugs which may save lives, restore normal functioning, or alleviate unbearable pain.

To maintain that balance requires public confidence in both the ability of the FDA to make approval or nonapproval decisions rapidly and the ability of private industry to conduct competent and scientific studies. That confidence has not been earned with DMSO. Its 18-year odyssey has made a travesty of the regulatory process.

I do not know if DMSO works or not, but with the hopes of so many Americans riding on it, with so many others already using it, I believe a definitive evaluation must be made, and made soon. Therefore, I have directed that the staff of the subcommittee convene a meeting as soon as possible among the FDA, the NIH, all the manufacturers interested in marketing this product. The purpose would be to determine what needs to be done and how it can be done, and to develop a timetable for doing it. I cannot promise those Americans who look to DMSO to cure their ills that it will turn out to be a wonder drug, but I can do and promise to end the wondering about it and replace it with some definitive answers.

Senator Schweiker.

Senator SCHWEIKER. Thank you, Mr. Chairman.

In recent months, there has been a resurgence of public interest in the potential benefits of dimethyl sulfoxide, DMSO. Although its only FDA-approved use in this country is for the treatment of a rare bladder condition, DMSO advocates have claimed that it is safe and effective for a number of other important uses, including arthritis and musculo-skeletal disorders, painful finger ulcers, athletic injuries, brain and spinal cord injuries. These are severely disabling conditions that cause great suffering to millions of Americans. About 15 percent of the population are victims of arthritis and related conditions alone.

Spurred by news accounts of its effectiveness, many people have turned to DMSO. Some have even begun to use industrial grade DMSO and products designed for animal use, without medical supervision, perhaps exposing themselves to serious risks. Thousands of patients have traveled to Mexico, where they receive preparations that may contain other drugs with potentially severe side effects.

Proper testing should establish whether or not DMSO is safe and effective. If DMSO works, it should be available in a safe form to those who can benefit from it. Americans should not have to travel

great distances or rely on industrial solvents to treat their pain. If DMSO does not work, the American people need to be informed so that they will no longer be victims of baseless wonder drug claims or run the risks inherent in the use of any drug.

Our country's drug approval system is based on rigorous, scientifically sound evaluation of studies designed to show that drug products are safe and effective. The purpose of the drug laws administered by the Food and Drug Administration is to insure that Americans are not exposed to unsafe or fraudulently promoted drugs.

In the past, however, our subcommittee has on occasion found that the integrity of the entire drug approval system has been jeopardized by faulty or even fraudulent data submitted to the FDA. As I have stressed before, these deficiencies, even though limited, are not tolerable. Drug sponsors have a responsibility to provide meaningful and accurate data to FDA. FDA is responsible for monitoring drug research and development activities and acting expeditiously to resolve any problems that are found, so Americans can rely with confidence on the drugs prescribed for them and bureaucratic delays do not hamper the availability of needed drugs that can relieve so much pain and suffering.

This morning, we will be examining the record of both FDA and drug sponsors with respect to DMSO. I hope we will be able to gain insight into the value of studies that have been done and the need for additional studies to be conducted promptly. We will also hear from patients who have direct personal experience with DMSO.

These are important issues. They are central to our drug approval system and to the protection of the American public. I commend Chairman Kennedy for his steadfast dedication in addressing these problems, and look forward to the testimony we will receive this morning.

Thank you, Mr. Chairman.

Senator KENNEDY. Senator Hatch.

Senator HATCH. Thank you, Mr. Chairman.

I am especially glad to see among today's witnesses several citizens who will be talking with us about their own experiences with the use of dimethyl sulfoxide.

The revival of interest in the use of DMSO as a treatment for arthritis and musc[illegible] disorders was not merely the continuing fallout of the recently broadcast CBS 60 Minutes program. Unsolicited testimonials offered by countless patients and many of their physicians attest to the therapeutic benefits they believe to be derived from this extract. The continued near total FDA ban on DMSO's use has, in itself, has become for many Americans a most recent cause for battle in the Federal regulatory war.

The handling of DMSO is one of the most important questions to be weighed by this subcommittee, and certainly one of the most timely. Some of my congressional colleagues have already introduced or cosponsored legislation to legalize its sale and the use of DMSO, regardless of FDA's objections or of the reservations of some members of the scientific community. Others, including Senator Packwood and myself, have sponsored legislation requesting further clinical study and investigation through the National Institute of Arthritis.

We all recognize the importance of preserving the integrity of the FDA process and of permitting to be sold to the public medicines which are not proven to be destructive or ineffective. At the same time, most of us also recognize the endemic bureaucratic problems created by large organizations, especially organizations as large as the Federal Government. As sincere and hard working as are so many at FDA, I suspect that these inherent organizational problems have a lot to do with the continuing controversy over DMSO's internment over these past 18 years. Certainly, it is one of the major questions to be answered here this morning.

There continue to be charges and countercharges of "clinical coverups, deceitful practices, and distortions of scientific data," and I am quoting here from several of the principal adversaries in this controversy. Such acrimony and the prevailing myths surrounding DMSO contribute nothing to the hard clinical investigation which must be undertaken, and undertaken very soon, in order that what healing power this sulfuric solvent has may be used for the benefit of all citizens and not simply confined to the people in those three States where it is presently legalized.

Dr. Stanley Jacob, whose name has become almost synonymous with DMSO, and the testimony to be given by Mr. Moyle of Research Industries, Inc., based in my own home State of Utah, promise to shed additional light on the matter.

The handling of DMSO is one of those issues uniting every member of this subcommittee. I feel confident in saying that our chairman, Senator Kennedy, our ranking member, Senator Schweiker, and all of us, want to see DMSO proven safe and effective to the optimal degree it can be determined to be so and, under such conditions, made available to those citizens wanting to use it.

Thank you, Mr. Chairman.

Senator KENNEDY. We will start off hearing from a number of individuals who have had experiences with DMSO. Let us start off with Daryle Lamonica. We are grateful for the presence of all of our witnesses, and Mr. Lamonica was good enough to come overnight from the west coast and will be leaving shortly to return to California. So we are very grateful for the special efforts that have been made by all the witnesses; we want to welcome all of them.

Mr. Lamonica, perhaps you could just tell us, when did you play for Notre Dame and when did you play for the Oakland Raiders, and why did you not treat the New England Patriots a little better? [Laughter.]

STATEMENT OF DARYLE LAMONICA, SAN FRANCISCO, CALIF.; SAM BELL, BLOOMINGTON, IND.; MURRAY BECKER, NEW YORK, N.Y.; PATRICK POTTER, BEAVER CREEK, OREG.; JEAN PUCCIO, WASHINGTON, D.C.; AND ILLY ROBERTS, FALLS CHURCH, VA., A PANEL

Mr. LAMONICA. I graduated from Notre Dame in 1963 and started my professional career with the Buffalo Bills, and then I was traded to the Oakland Raiders, where I had my first experience with DMSO. It was on a jammed thumb on my throwing hand in practice on a Wednesday.

Senator KENNEDY. When was this approximately; what year was it?

Mr. LAMONICA. 1967, September; we were in league play at the time.

Dr. Graham Reedy was one of our team physicians at the time, and he had had some experiences with DMSO on other professional athletes and athletes. And I came into the training room; my thumb was swollen to the point where I could not bend it, could not grip a football. And I had heard other players talking about DMSO.

One thing that is a characteristic of it, at least at that time for anybody using it, is that it did not do much for your social life because of a smell that it put off. It was more like dead clams. Anybody got in the huddle or anybody walked into the training room, you knew was using this particular DMSO.

But the doctor asked me if I would like to try it, and he said that he felt that it would take the swelling out. I did; I put it on. It was a clear alcohol substance. We put it on my thumb, and it burned. It did blister the skin; he told me that it might. I watched it blister before me, and it almost started to smoke. The swelling actually went down right before my eyes, and I really couldn't believe it. Within 5 or 6 minutes or so, my skin was back to normal and the majority of the swelling was down. It was still tender to some degree. I was able to throw a football the next day and was able to compete that particular Sunday.

As professional athletes, we do not live in fear of major injuries, but it is something that we have to live with. We are susceptible to pulls, strains, and sprains are the biggest things.

I had a chance to use it many times after that. On a strained knee, where I had strained my ligaments and I had a lot of swelling, again I used it. It took the swelling out of my knee. I was able to participate that following week. I had a sprained ankle. I was able to put it on my ankle to take the swelling out, to be able to tape it up and run on it the next day. I also used it on a lower back sprain that I received. My wife, the nurses said, was one of the only ones who would come into the room. That is the only fault that I found with DMSO.

From my own personal experiences, it did take away the pain. I called it the miracle drug. I am not qualified to determine what it is and what it has in it, but I do know that it did take the swelling out and it did take the pain out, and I was able to compete.

There were other ball players on our team who used it when they had injuries: Tom Keating; Ben Davidson; Jim Otto, who is being inducted into the Hall of Fame this coming month; and Pete Banaszak. There were several of our guys that were All Pro, all veterans, that used it. I think without that they would not have been able to compete. I know I could not have been able to compete that following week without the use of DMSO.

Senator KENNEDY. As compared to other treatments that you might have taken for the injuries which you experienced—you have obviously experienced a number—how did the resolution of those injuries compare when you used this particular drug to using the other techniques?

Mr. LAMONICA. Other techniques, you used, of course, ice, iced it down and try to get the swelling out and then go to a whirlpool treatment, heat treatment to try to get it out. But, normally, on a normal sprain, it was my experience that it takes 4 or 5 days to get the swelling out, and the soreness is the worst thing. Once you get the swelling out, you have a chance you can tape it; if it is a sprained ankle, tape it back and lock it in position where you are able to move around on it.

With the DMSO, I was able to compete to some degree and work out the following day or in a couple of days. Professional athletes, or any athletes, we are not blessed with the time where you can go take 2 or 3 weeks off from an injury, and getting back onto the field—maybe that is the competitiveness in us, but we hate to miss any time.

Senator KENNEDY. Mr. Lamonica, you have indicated that there were a number of members of the Oakland Raiders team that used this. Was it for the same kinds of injuries which you have outlined here?

Mr. LAMONICA. Yes. They were mostly pulls and sprains, hamstrings, sprained ankles, jammed fingers—jammed fingers were with linemen and receivers—and hamstring pulls, and knees. Those were the most. And, of course, my jammed finger.

Senator KENNEDY. Those were the usual injuries for which it was used?

Mr. LAMONICA. Yes.

Senator KENNEDY. And to the best of your knowledge, were the other professional teams using it, your friends on some of the other teams as well?

Mr. LAMONICA. Yes. I know one friend I was very close with, Dave Williams, who played with the San Diego Chargers and was an outstanding wide receiver, used it frequently and had the same results. He is very pro-DMSO.

Senator KENNEDY. Mr. Sam Bell, you are the track coach of Indiana University, is that correct?

Mr. BELL. Yes.

Senator KENNEDY. How long have you held that position?

Mr. BELL. I have been at Indiana University for 11 years.

Senator KENNEDY. And where did you coach prior to that time?

Mr. BELL. The previous 4 years to that, I was at the University of California at Berkeley, and the 7 years previous to that, I was at Oregon State University in Corvallis, Oregon. I came into contact with this while I was at Oregon State University.

Senator KENNEDY. I see. So you have been coaching how many years? If you add all those up together, it is a long time.

Mr. BELL. I have been in college coaching for 22 years, and I coached high school 8 years prior to that.

Senator KENNEDY. And when did you first come in contact with DMSO?

Mr. BELL. My first experience with it was in the spring of 1963. At that time, I had two athletes who were having leg problems; one of them was having a tendon problem and one was having a hamstring problem. Their names are Morgan Growth and Norm Hoffman, and they were both world class 800 meter men. I was concerned because they were both potential scorers in the NCAA.

We had a chronic problem with both of them, and what we were doing trainingwise was having no effect on them. I had read in the paper some of the things that Dr. Jacob had discovered with DMSO, and I called him at the University of Oregon Medical Center and asked him if I could bring these two athletes up to see him. And we went up there to visit with him, and he examined them and gave us some DMSO to use and told us how to use it. We used it topically, or we put it on the skin.

In Morgan Growth's case, he had an achilles tendon, which is a chronic injury which seems to never right itself when you really hurt one. But that spring, he was the NCAA champion in the mile run at the University of New Mexico. And Norm Hoffman, the other athlete who had a hamstring problem and really could not even train, ended up being the NCAA champion in the 880 that year.

I had a little of this left over, and that fall, I was doing some work in my yard and sprained an ankle grubbing out a stump, and it was an old injury from football days in college, and I ended up deciding maybe I ought to experiment with it myself and I gave myself six treatments over a period of 3 days. My ankle, because of it being an old injury, always swelled up very badly whenever I sprained it again. Within 3 days, I had no swelling, no soreness, no discloration; I could do anything I had been doing on it.

My next experience with the drug really came in the fall of 1964. At that time, we were running a 2-day Olympic trial in track and field, and a young man who jumped for us at Oregon State named Daryll Horn, who was the No. 2-ranking long jumper and No. 2-ranking triple jumper in the United States at that time——

Senator KENNEDY. What was his specialty?

Mr. BELL. He was a long jumper and a triple jumper.

Senator KENNEDY. Triple jumper being what?

Mr. BELL. Well, in the common nomenclature, maybe it is called the hop, step, jump.

Senator KENNEDY. OK.

Mr. BELL. It is a very difficult event; it takes very good legs.

Daryll had graduated from Oregon State in the midyear in 1963 and had gone into the Air Force, and he was on detached duty prior to the Olympic trials training at Stanford University. And I went to Southern California for the Olympic trials and asked the coach from Stanford University, Mr. Peyton Jordon, where Daryll was, because he was not in camp yet, and he said, "Well, I hate to tell you this, but he had a massive hamstring pull on Monday," and he said, "He is staying at Palo Alto to try to get treatment as long as possible before he comes down here, but he said there is no way he will be able to compete."

So I immediately got on the phone to Daryll at Palo Alto and visited with him, and he said, "Coach, I am black and blue from the gluteus," which is the big butt muscle, "to down below my knee," and he said, "I cannot walk without a limp." I said, "Get on an airplane and get down here as fast as you can." I called Dr. Jacob in Portland and asked him if we could get some DMSO to treat Daryll, and he said, "If you can have someone pick it up, we will get it." So I had a friend go to Dr. Jacob's office and pick up

some DMSO, and he took it to an airport and found a stewardess who would take it to L.A., and I met the plane.

Daryll got down there, and we began treatment on him on Thursday morning, and the trials were on Saturday afternoon in the long jump. We really dosed him. He ran his roommate out of the room from the odor, and he got some skin irritation. With about half the people I've used DMSO with, they have come up with some kind of skin irritation. We have never had any blistering, such as Daryll has described, but we have had skin irritation.

To make a long story short, we practically bathed Daryll in that for 2 days, and on Saturday afternoon, he missed the Olympic team by a quarter of an inch. On Sunday, we went back and competed again, and we continued to treat him over Saturday night and Sunday morning, and he went back and competed again and he missed the Olympic team in the triple jump by a half-inch. He obviously did not come back to where he was, but the fact that he was even able to compete, I thought was a minor miracle. He competed with no discoloration of the leg; it was totally gone in 2 days, and the soreness was gone. I think, obviously, the strength was not quite back there, but the fact that he was able to operate at all is an amazing thing.

Just to skip some time frames from 1964 until the present, in the spring of 1979, we had a sprinter named Bill Copeland who had had some chronic hamstring problems and he got a massive muscle pull in mid-April. Our trainer said 6 to 8 weeks and did the regular treatment. I decided that it was Bill's senior year, that we could not afford to wait that long, and Bill did not want to wait that long. So we used DMSO on him, and he ended up placing in both the 100 and 200 meters at the Big Ten championships 5 weeks after the massive muscle pull, and he had been competing for 2 weeks prior to that.

The things that I have found with it is the fact that it is very effective with new injuries such as pulls and strains and sprains; it is also effective with contusions that are very new; it does not work as quickly with things such as tendons, where the circulatory system is not as effective as it is in a muscular area, but it does work—you just have to have a little more patience. I have been around it enough that when I step close to anyone who is using it, I can tell that it is there. Our athletes themselves joke about the fact that they will have no dates for a period of time while it is being used, because, as Daryle says, it really does affect social life.

But the healing qualities of it are such that people in athletics, where it is important to train constantly as well as to be able to compete—and maybe the training is more important because of what happens down the long road—can be put into operation and they do not miss time in training.

Senator KENNEDY. What is your experience from talking to other coaches? How widespread is it?

Mr. BELL. It is not real widespread with coaches because it is not available to them as a general rule. The reason I happened to be able to use it is the the fact that I happened to be living in Oregon when it was discovered and got to know Dr. Stanley Jacob and spent some time with him and have used it from Dr. Stanley Jacob ever since.

It was used by our training staff at the University of California when I was at Berkeley—not on a real wide basis, but it was used there.

As an aside, I would tell you that within the last week and a half, I talked to someone in my hometown who said, "I have got a problem with a leg that I have hurt in tennis," and he said, "I am going to go get some DMSO." I said, "Well, where are you going to get it?" He said, "I am going to my vet."

Senator KENNEDY. Tell us a little bit about that? Why do they go to their vet?

Mr. BELL. Well, veterinary medicine can use it as a prescription on animals and, therefore, it is readily available to them. It is obvious from the treatment of animals in certain situations that it is beneficial to muscle injuries, and things like this. Therefore, a veterinary has access to DMSO.

Senator KENNEDY. Mr. Murray Becker, we welcome you. How old are you, Mr. Becker?

Mr. BECKER. Can I take the Fifth? [Laughter.]

Senator SCHWEIKER. Good answer.

Mr. BECKER. Eighty-five.

Senator KENNEDY. Eighty-five?

Mr. BECKER. Yes, and at my age, I have no connection with the athletic industry. [Laughter.]

Mr. BECKER. I have been practicing law for 53 years, and still continuing to do so on a daily basis. I think to appreciate the dramatic results that I have had from DMSO, I would have to trace quickly and briefly the origin and history of my problem.

It goes back some 30 years, or close to it, when I first developed tremendous pains in the calves of both my legs, combined with what are known as vacillations. That is jerky movements of the muscles, which go constantly; it never stops; maybe when I am sleeping, they stop, but I would not know. The result was that after this went on for a number of years and became quite troublesome, to the point where I could not sleep, it kept me awake, I went to an orthopedic doctor who told me that I was in the wrong place, that what I needed was a neurologist, and he referred me to a man by the name of Isadore Wexler, who was very prominently known internationally; he is the man who wrote the standard textbook on neurology used in all the medical schools.

I was under his care for about 5 or 6 years, going through all kinds of tests, hospitalized three times for about a week at a time for study and tests, and the net result of it was zero. When I was all finished, he had no answer, no remedy, no cure.

I went along with it for a number of years, and then it was my good fortune, when I served as a trustee of New York University, to meet Dr. Howard Rusk, who is the creator and founder of the famous Rusk Institute of Rehabilitation. I told Howard my problem, and he took me under his personal care. For a period of over a year, in conjunction with his internists and his neurologists, they studied me—all sorts of examinations. Every month, they would put me on a new experimental drug to see if that would help, and the net result again, after the year was up, was zero. He then put me on a therapy program at the institute, where I went 2 or 3 days a week for treatment and therapy. That brought no results.

By this time, it was getting worse; it was progressively worse, and I was unable virtually to walk. If I walked more than a block, 200 feet, I would become paralyzed with pain. I would have to sit down in the street for 20 or 30 minutes until I was able to move again, or walk into some shop and ask permission to sit there for a half hour or so until I recovered.

Finally, my physician sent me to a neurologist by the name of Houston Merrick at Columbia Presbyterian in 1972, and he did a different type of electrical study and came up with an answer, the first diagnosis I had ever had after all those years. The diagnosis was that the cells in my spine were atrophying and were getting progressively worse, and that there was no cure for it, nor was there any way of relieving the pain. When the report of Dr. Merrick went to my personal physician, he, in turn, put me on Percodan, a heavy pain-killing drug. Up to that time, I had never used anything but Bufferin for relief.

Well, the Percodan was fine, except that it only worked for about 2 hours after you took it. It took about a half hour before it started to take effect, and then it would hold me for about 2 hours, and then the pain would start all over again. There was just nothing to be done about it; I just had to struggle through it.

In my profession, since I sit on a number of boards of directors throughout the country—Boston, Philadelphia, Chicago—I travel a great deal. My travel consists of a limousine meeting me at the door, getting me to the airport and getting me into a wheelchair. I want you to know that when I came here today, it is the first time I have ever got into an airport without a wheelchair in the last 15 years, I would say.

Finally, I saw the program on "60 Minutes". I followed up on it. I got an appointment with Dr. Jacob, and the most dramatic thing in the world happened. I saw him about 5 one afternoon; I think it was June 4. I walked in; I had all of my medical records; he read them. After studying them, he said, "I am sure I cannot, at your age, bring back the cells in your spine; they are gone, and they are probably going to continue to go. But I do think, since I have had quite a great deal of success in the spine area, I can help your pain." He gave the DMSO, told me how to use it.

I went back to the hotel and used it that night. I used it the next morning, and that morning, I had an appointment with him at 11. Before I went to him, I walked from the Benson Hotel to the Myer and Frank Department Store, which I would say is about 6 blocks; I did some shopping, walked back to the hotel. I have never had a drug since the day I saw Dr. Jacob; I have not taken any Percodan, not even Bufferin, and I have had no pain.

Now, when I got back, I went to my personal physician, who happens to be a full professor of internal medicine at NYU Medical School, and I told him the story. He not only approved of what I did; he said, "But I do want to do one thing. I want to test you, because this does get into the blood stream, and I want you to take a series of blood tests, a full battery of blood tests." I have had two of those already; the results were all negative.

In addition thereto, I had read in the literature that there was something about this thing affecting the eyes of animals. So I promptly made an appointment and went to see my eye doctor. He

examined me; he went right to the books to make sure he knew what DMSO was, and he said, "All I can say is your eyes are no worse than they were; if anything, they happen to be a little better."

It is a dramatic story, and it is almost unbelievable.

Senator KENNEDY. You answered the question, but I want to just make sure for the record. Did you use any other drug during any of this time?

Mr. BECKER. Since I saw Dr. Jacob?

Senator KENNEDY. Yes.

Mr. BECKER. I have used no drug of any kind.

Senator KENNEDY. There is a different form of DMSO, is there not?

Mr. BECKER. Yes. I think it is an improved form, because I have had no odor. In fact, I have had no side effects.

Senator KENNEDY. Dusa-Sal; is that Dusa-Sal?

Mr. BECKER. I beg your pardon?

Senator KENNEDY. Dusa-Sal; is that familiar to you? That is not familiar to you?

Mr. BECKER. No.

Senator SCHWEIKER. You say you had no side effects, Mr. Becker?

Mr. BECKER. No, none. Dr. Jacob said, "You might get some burning sensation, or you might get an itching. My advice to you is, do not run into the shower and wash off the DMSO; stay with it; it will help you." But I have never had a burning nor an itching, or any sensation of any kind.

As a matter of fact, I started using it twice a day. For almost a month now, I have been using it only once a day, and in the last week or so, I have been skipping a day.

Senator KENNEDY. Mr. Potter, where do you live?

Mr. POTTER. I live in Beaver Creek, Oreg.; it is about 25 miles south of Portland.

If you would like, I have some doctors' reports here that I could let you have.

Senator KENNEDY. What are those?

Mr. POTTER. Doctors' reports.

Senator KENNEDY. Fine. We will just include them as part of the record.

[The material referred to follows:]

...CIANS AND SURGEONS

ORTHOPEDIC AND FRACTURE CLINIC P.C.

...ST VINCENT MEDICAL CENTER
9155 S.W. BARNES ROAD
PORTLAND, OREGON 97225

PHONE 297-3511
BOOKKEEPING 297-5041

HOWARD L. CHERRY, M.D.
CHARLES A. FAGAN, M.D.
SAMUEL F. GILL, M.D.
DAVID S. WIDDOW, M.D.
ARTHUR L. HALSEE, M.D.
J.D.V. BUTLER, M.D.
JOHN D. HATHAWAY, M.D.

December 26, 1979

Tobin, Crawford & Mikolavich, Inc.
P.O. Box 937
Medford, OR 97501

RE: Patrick Potter
Claim No. 1551425
DOI: 11-25-75
Emp. Fought & Company, Inc.
File No. 61730H41P

ATTENTION: Sue Worthington

Dear Ms. Worthington:

Thank you very much for your letter of December 18, 1979. I do appreciate your authorizing this man to attend the Northwest Pain Center to see if he can be helped. You inquire about the office calls of October 26, and November 28, 1979.

This man had been hospitalized by me being admitted on 9-16-79 and discharged on 9-30-79. He was in St. Vincent Hospital with severe low back strain and possible disc. I had him seen by Dr. Berkeley, neurosurgeon, who did a myelogram and did not show evidence of a herniated disc. Mr. Potter did show some gradual improvement by the time he was discharged on his 14th hospital day though he was still symptomatic.

I next saw him on October 26, 1979. He was quite sore. He ran out of pain pills and was hurting more than usual. He stated that he had a hearing the week previous but did not have results of it yet. He was sore in his low back and has considerable muscle spasm.

I prescribed Tylenol #3 and Soma for him. He indicated an interest in seeing Dr. Jacobs at the Medical School in regard to DMSO.

I next saw him on November 28, 1979. He was very sore. He was using DMSO and is in contact with Dr. Jacobs' office. He was quite sore after his myelogram and that did improve to a degree and then got worse again. He has not been able to work to date. He takes Tylenol #3 and Soma on my prescription.

Physical examination reveals a husky man. He has a 4", midline low back scar. He is tender at the lumbosacral level. He bends to reach just past his knees. Backward and side motion are less than 50% of normal. He stands with his right hip and right knee flexed. He walks with his cane protecting the right leg. The circumference of the calves is 14" on the right and 14½" on the left. Circumferences of the thighs are 21" on the right and 21½" on the left. Straight leg raising is to 20 degrees on the right and 45 degrees on the left. Hip flexion is painful on the right. Faber's test is normal. Sensation is reduced in the right thigh and base of the right great toe. Knee kicks are 2+ bilaterally.

...EDIC AND FRACTURE CLINIC, P.C. ... ST. VINCENT MEDICAL CENTER PORTLAND OREGON 97225

Tobin, Crawford, etc. Page 2 December 26, 1979

RE: Patrick Potter

Ankle jerks are 1+ bilaterally. Strength of the great toes is excellent. He is not tender at the sciatic notch or popliteal areas. He can walk on his heels but hurts to walk on his toes.

It is my impression that this man has severe residual pain in his back and right leg from previous disc treated by laminectomy on two occasions.

I renewed his Soma and Tylenol. I am very happy that he is going to the Pain Clinic and sincerely hope it does help him.

Very truly yours,

Howard L. Cherry, M.D.

HLC:ak

/ Pat Potter
[illegible]

68-489 O—80——2

ST. VINCENT HOSPITAL and MEDICAL CENTER
Portland, Oregon

CONSULTATION REPORT:

DATE: 9/24/79

CONSULTANT: Dr. E. W. Berkeley

POTTER, Patrick John
465510 809-1
Dr. H. Cherry
Adm 9/16/79

19015

Referred for consultation concerning:

Consultant's findings and recommendations:

Thank you very much for asking me to see this unfortunate young man. He is a 37-year-old right-handed man who was a welder by profession in the past.

Around November, 1975, he lifted up a heavy saw horse and the following morning he had severe low backache and pain in the right leg radiating to the thigh, calf and ankle, as well as the toes. The patient was first seen in Kaiser Hospital and subsequently he was seen by another doctor who did a myelography on him in 1975, December. From then onwards he was referred to Dr. C. Hill, neurosurgeon in Providence Hospital, where a second myelography was performed in March, 1976. Following this Dr. C. Hill operated on the patient's back and removed a prolapsed intervertebral disc. Postoperatively the patient remained symptomatic with severe pain in the right leg, and he had "rhizotomy" performed by the same surgeon around June or July, 1976. He still remained symptomatic and was admitted again under the care of Dr. C. Hill at Providence Hospital around late November, 1976, when a third myelography was performed. Following this the patient had a second back operation and some scar tissue removed. This operation was very successful and relieved almost 90% of the patient's previous symptoms. After a few months of recuperation the patient was able eventually to return to work. Apparently he retrained for a salesman rather than to continue as a welder.

He was quite happy and practically asymptomatic until March, 1979, when he started to develop again episodes of acute pain in the right leg radiating again along the thigh and the calf as far down as the toes, and precipitating falls as the patient was unable to control himself during these episodes. He had, in fact, several falls as a result of these attacks. He was seen again by Dr. Curtis Hill and was then sent to the "Callahan Center" in Wilsonville where he had physiotherapy and rehabilitation to no avail.

The patient's symptoms became, in time, increasingly more severe and intolerable. About a week ago last Sunday the patient had excruciating pain in the right leg and was admitted to this hospital under the care of Dr. Cherry. Weeks of traction has not contributed to any significant improvement. His main complaint, constant pain in the right leg from the hip down to the thigh, calf and ankle, and involving all the lateral toes, both at rest and much worse on standing or bearing weight on the right leg. He has no cough or sneeze aggravation. He is unable to sit for long and has to change position constantly and he is totally unable to bend or lift anything. He has no sphincteric problems. He has at times, paresthesia in the right calf, and in addition he complains of dense sensory changes in the anterior aspect of the right thigh, just above the knee. He denies any weakness in the legs and he emphasizes that the reason why he falls is the sharp episodes of acute right sciatica which make him lose control of his right leg.

PAST MEDICAL HISTORY: Irrelevant. No diabetes mellitus. No other systemic illness.

Consulting Physician

465510

CLINICAL EXAMINATION : He is a well-built man.
HEAD AND NECK: Revealed no external abnormalities. Carotids pulsate in the neck symmetrically with no bruits.
CNS: Mental state and speech normal. Dominance right-handed.
CRANIAL NERVES: No abnormalities detected throughout.
UPPER LIMBS: Power, tone, sensation and coordination normal. Triceps, biceps and supinator reflexes present and symmetrical. Peripheral pulses present and symmetrical Adson's maneuvers negative.
LOWER LIMBS: No wasting or fasciculation. There is no weakness. Straight leg raising is 65 degrees on the left, causing cross-pain to the right buttock and right hip. On the right it is similarly about 60 to 65 degrees. The Lasegue's sign is positive. There is an area ov sensory diminution above the right knee on the anterior and lateral aspect of the thigh which would correspond approximately to the L3 dermatome.

The remaining dermatomes, however, have normal sensation and joint position and vibration senses are also normal. The knee and ankle jerks are present and symmetrical and the plantar responses are flexor. Pulses in both lower limbs are normal and symmetrical.

Examination of the back reveals a flattened lumbar lordosis and a midline scar. There is some tenderness in the lumbosacral region, radiating to the right sacro-iliac joint of the right buttock. Flexion and extension of the lumbar spine are extremely limited and painful, and these were not pursued any further because of the discomfort caused to the patient during this examination.
CHEST AND ABDOMEN: Unremarkable.

CLINICAL IMPRESSION:
It is difficult to correlate the patient's pain to a particular level, especially with L3 dermatome sensory loss, with no other focal localizing neurological signs. I feel that a Metrizamide lumbar myelography should be performed to clarify this further, but should this prove negative, I do not think that any surgical procedure would be indicated to alleviate this patient's symptoms.

Once more, thank you for asking me to see this patient.

Dictated by E. W. Berkeley, M. D. 9/24/79
Transcribed by md 9/27/79

cc: Dr. E. W. Berkeley
Dr. H. Cherry

ST. VINCENT HOSPITAL AND MEDICAL CENTER
Portland, Oregon

OPERATIVE RECORD

WC
POTTER, Patrick John
465510 809-1
Dr. H. Cherry
Adm 9/16/79

19015

DATE OF SURGERY: 9/25/79

PREOP DIAGNOSIS: Post laminectomy and discectomy status, with scarring at L5-S1, on the right side.

POSTOP DIAGNOSIS: Same.

OPERATION: Metrizamide lumbar myelography.

SURGEON(S) Dr. E. W. Berkeley

The patient was positioned prone on the x-ray table and the usual skin preparation and draping were carried out. A lumbar puncture was attempted first at the L3-4 interspace but the canal was very narrow and the needle which was 20 gauge could not be directed into the canal, but was diverted right or left. In view of this an attempt was made at L2-3 with a #18 gauge needle. Here again, great difficulty was encountered because of the narrowness of the canal and the pain experienced by the patient, in spite of midline approach and local anesthesia. Eventually, Dr. Devine managed to introduce the needle into the interspace and clear CSF was obtained and sent to the laboratories for routine investigations. 18 cc. of 180 concentration Metrizamide was then introduced into the subarachnoid space and the needle was withdrawn. The appropriate films were taken and these revealed asymmetry of the nerve roots at L5-S1, the abnormality being on the right side, with the nerve root not filling there and appearing rather irregular, suggestive of scarring which would be compatible with his previous surgery. No other lesion was demonstrated.

Dictated by E. W. Berkeley, M. D. 9/25/79
Transcribed by md 9/29/79

cc: Dr. E. W. Berkeley
Dr. H. Cherry
Workmen's Compensation

Anes S 1115 Anes E Local
Oper S 1120 Oper E 1150

Signature of Surgeon

Donald Semmens, O.D.
Optometrist
10180 S.E. Sunnyside Road
Clackamas, Oregon 97015
(503)653-4411

KAISER
PERMANENTE
MEDICAL CARE PROGRAM

To whom this may concern;

Patrick Potter was examined in my office February 12, 1980.

In comparison to his previous corrective lens prescription his vision has remained stable. No significant visual or ocular health changes had occurred since his previous examination.

If I can be of further assistance please contact me.

Sincerely

Donald J Semmens OD

Pat Potter
[illegible]
[illegible]

Mr. POTTER. My first encounter with DMSO was last fall. It was after I had had my fourth myelogram for my back. I have had two surgeries for laminectomies due to an injury on the job. I had been told after the fourth myelogram there was nothing that they could do for me, I was going to have to learn to live with the pain and with the fact of the leg giving away. The scar tissue had—what they found in the myelogram—had built up around the sciatic nerve to the point where it had cut it off once in a while, and my right leg, it pulled up under me and I would fall to the ground, so therefore I was using a cane.

These reports will kind of show you how much medication I was on—a considerable amount of Tylenol 3 with codeine, and muscle relaxers, Soma. And when I went to use the DMSO, when I went to see Dr. Jacob, I started using the DMSO topically, and about 4 weeks later, I received my first injection. Since then, I have had 24 injections of it, and I am pain-free now.

After about the third injection, I leaned my cane up in the corner. After about the sixth injection of it, I quit taking medication, and I have quit completely; after about the ninth injection, I completely quit the medication, and I have not taken anything for it since then.

Senator KENNEDY. What have the physicians told you about your condition?

Mr. POTTER. The physicians had told me that there was absolutely nothing that they could do for my situation; that they could operate again, but in another year to a year and a half, the scar tissue would form again to the point where it was and I would be back in the same situation.

Senator KENNEDY. What do they tell you now? Have you seen those same doctors?

Mr. POTTER. I have not had to go back to see the doctors.

This will give you my range of motion that I had before I went to see Dr. Jacob [indicating], and I have got the same range of motion that anybody on the panel up there has now.

Senator KENNEDY. How did you learn about DMSO?

Mr. POTTER. I learned about it through a friend of mine that had been going to see Dr. Jacob. He had received several shots of it, and it was doing him some temporary good. However, his problem is a bone problem, and it was relieving the pain temporarily for him, but the difference——

Senator SCHWEIKER. Did you experience any side effects at all, Mr. Potter?

Mr. POTTER. I could clear a city bus in 30 seconds. [Laughter.]

The odor is tremendous when you get an injection of it.

Senator SCHWEIKER. That's the worst you got?

Mr. POTTER. Yes. When I use it topically, there is a good itch; it is a real strong itch, but that is all.

I used to be a welder, and my wife came out to the shop one evening when I was welding up a small trailer, and she laid her hand down on something that had just lost its redness, and the smoke rose from where she put her fingers down on there. She ran into the house and she grabbed the DMSO and poured it over her fingers, and they never even blistered; they never did hurt her. So, as well as the scar tissue softening, it does good for burns, too.

Senator KENNEDY. Mrs. Puccio, as I understand it, you were diagnosed 9 years ago at the Walter Reed Hospital for scleroderma, is that correct?

Mrs. PUCCIO. Yes.

Senator KENNEDY. And what did the doctors tell you about the disease at that time?

Mrs. PUCCIO. When I went to Walter Reed, I stayed a week. I had, before then, been going for about a year and a half to the military doctors, and they did not know what my problem was. When I finally got to Walter Reed, I stayed a week and they did muscle biopsies and nerve blocks, and I was examined by 30 doctors and several civilian consultants. They told me that I had scleroderma, which I had never heard of.

So I said, "OK; fine. What are we going to do about it?" He said, "Unfortunately, there is nothing you can do about it." I said, "No medication?" He said, "No. The best you can hope for is a wheelchair, and within a short time, probably die." And, of course, I knew that was not going to happen. That was 1971.

I went from doctor to doctor to doctor. I finally found Dr. Jacob through a lady in Pennsylvania. I called and went to Portland. Dr. Jacob examined me, and he verified the disease. At that time, I was becoming Oriental-looking; my skin was being pulled back. I was having difficulty breathing and walking and eating. He put me on topical DMSO, but it burned my skin, since scleroderma has a tendency to make your skin tissue thin.

Senator KENNEDY. Just so we can get a little better idea of scleroderma—I do not know whether all of us are completely familiar with the outward signs of it; you have described some of those—maybe you could tell us just a little bit more about, for example, why you had difficulty opening your mouth or difficulty eating.

Mrs. PUCCIO. Because it constricts your tissue; it thickens the tissue, and it makes your skin so tight you cannot move. It was difficult for me to drive; it was difficult for me to turn the ignition in my car or turn. It was just very difficult.

Senator KENNEDY. Even to eat, as you have mentioned?

Mrs. PUCCIO. Yes, yes. I have a letter here from my dentist. He could not do any dental work on me for a while. Now, I can open my mouth like anybody else does.

But to go back, I went to Dr. Jacob, and he gave me the medication, which I brought back to Virginia. I painted it topically, but it burned my skin. I called him back, and he said, "Let us try taking it orally," so I started taking it orally. Within about 6 months, my condition reversed almost immediately.

I am a hair stylist. I work 12, 13 hours a day. I can do anything anybody else can now. Unfortunately, I have to be on that drug for the rest of my life. I have a civilian doctor in Alexandria who is well aware that I am on DMSO. I take no other drug. He sees me probably—at first, every month, and now, every 5 or 6 months. It is really not necessary for me to go to see him any longer because I feel really great.

Senator KENNEDY. Have you had any side effects of the drug itself?

Mrs. PUCCIO. I have had none.

Senator KENNEDY. You also are taking the new drug, 87-2, is that correct?

Mrs. PUCCIO. Yes.

Senator KENNEDY. What is that?

Mrs. PUCCIO. That, you paint on topically, and it is almost odorless-free. You paint it on your skin, and by morning, the odor is gone.

Senator KENNEDY. I see; OK.

Mrs. PUCCIO. I am extremely conscious of the odor, and when I drink it, I do not go out. I drink it on Saturday, and I am not out of that house until Monday evening, because I am conscious of it.

Senator KENNEDY. Have you had any eye examination since you began taking it?

Mrs. PUCCIO. Yes, every year, and I have had no problems with my eyes, and I have been on the drug for 7 years.

Senator KENNEDY. Ms. Roberts, as I understand it, you strained your back riding a bicycle some 3 years ago, is that correct?

Ms. ROBERTS. Well, I had a pulled muscle. I went to an osteopath. I did not know much about osteopaths, so I went to an osteopath and he said, "You have a pulled muscle." So he gave me a treatment which I was not familiar with. He cracked my spine. In 2 days, I went back to him; I came back with a terrible pain in my upper spine, and I went back to him and he gave me the same treatment a second time, and I could not walk anymore.

So I went to an orthopedic doctor, and he sent me immediately to a neurosurgeon, to the Naval Hospital, and they said, "Go to bed; you have a herniated disk," but they did not give me a myelogram that time, because it is too dangerous. So I was in bed for 2 months, and after that, I had some therapy, but I kept constantly having pain, chronic pain. It was unbearable, and I complained all the time; I went all the time back to the neurosurgeon.

So, in the fall, I went to another doctor, and they put me on Napacin because I complained. I had a broken blood vessel from that, so I stopped that immediately—in my eye, that is. Then I asked for some therapy, and the therapy made it worse. I had a tremendous attack before Christmas. I went back to the neurosurgeon, to Bethesda. They were going to give me a myelogram, but it was Christmas, so they postponed it until after Christmas. But I changed my mind and I went to Georgetown to a neurosurgeon, a civilian. He gave me a myelogram and they said I had two herniated disks, but they were overcrowded after Christmas in Georgetown and all the hospitals, so they sent me home and said to come back in a couple of months, do some exercise. The exercise aggravated it.

Then I went back in March, and he said, "OK. We operate now," and I said, "Well, I have some appointments with a dentist and also an eye doctor." I thought I would not tell him I was going to have some acupuncture, which made it worse. Then I heard about DMSO on 60 Minutes. I called the committee, and they told me some doctors in Florida. I could not go to Oregon or Las Vegas, because they have treatments there, too; it was way too far; I could not move that much; I was in bad condition.

So I went to Florida. Actually, I called the doctor in Florida and made an appointment. He gave me the price. It was fantastic. It was $1,374.

Senator KENNEDY. How much?

Ms. ROBERTS. $1,374 for four treatments. I had a physical, which was a very quickie, and four intravenously, and I took a bottle, a pint home for $200. But I knew what I was paying, and I think it is very wrong that people have to pay that much money and travel that far. And I urge this committee to really pass this, because there are a lotta lotta people who should have that drug.

I am really not crying anymore. I cried every day for 3 years because I had terrible pain. I maybe was not in a condition like you were, but I have no reflexes in my legs. I have two herniated disks, but I am not crying anymore. I can write a song about DMSO—smile.

Senator KENNEDY. How did you hear about it?

Ms. ROBERTS. Well, actually, I heard a year ago from a chemist, a Government chemist; he is retired now. He told me, "Rub some DMSO on your back," and he said to get it from a veterinarian. So I called all the vets up. I said, "My son has a dog; he needs DMSO," but he was not going to give it to me. So, then, that is the way I started. And this chemist has been using it for 20 years. His wife has psoriasis; she has been cured with it. So that is the way I heard about it.

By the way, I have glaucoma. I cannot take much. I cannot take any other drug. I have no side effects. In fact, I can drink it straight. I drink it twice a day, and I rub it on at night, and I am feeling great. I am not completely cured. They told me it will take quite a long time, because I have a little nerve compression.

Senator METZENBAUM. Did you have the glaucoma before?

Ms. ROBERTS. Yes, I did. I have had it for over 10 years.

Senator METZENBAUM. Has the doctor indicated that—

Ms. ROBERTS. No, I have not seen the doctor yet, but I will probably be in good shape when I go to him.

Senator METZENBAUM. It has not affected your eyes?

Ms. ROBERTS. Not at all. I see very well.

Senator KENNEDY. What was the cost that the rest of you paid for your treatments? Mr. Potter?

Mr. POTTER. My insurance company from the workmen's compensation is catching the bill for it. I have very limited knowledge of how much it is. I think it was approximately $700 for the 24 injections that I have had.

Senator KENNEDY. Do you remember, Mr. Becker?

Mr. BECKER. There has been no charge of any kind either for Dr. Jacob's service or for the material which he has given me. However, there is a foundation which supports this program, the John C. Higgins Foundation. I contributed to that, and I have gotten quite a number of my friends to do likewise.

Senator KENNEDY. I see. How about Mrs. Puccio?

Mrs. PUCCIO. I have paid nothing for the drug. I also contribute to the foundation. Dr. Jacob has not charged me anything in the past 7 years, and he always sees that I have the medication.

Senator KENNEDY. Mr. Bell, Mr. Lamonica, I suppose the athletic——

Mr. BELL. Actually, we have never paid anything for the drug. Dr. Jacob has always given it to us, and we have just used it in that capacity.

Senator KENNEDY. Daryle?

Mr. LAMONICA. Dr. Reedy acquired it.

Senator KENNEDY. Through the organization.

OK. This has been a very impressive and important testimony that you have given us here today. You have traveled a long way to tell us about this story and what it has meant to you as individuals, and I think that it has been very, very helpful testimony to the Committee.

Mr. BECKER. I think, Senator, I would like to make one observation. I think the sad part of it is that this thing is being bootlegged all over the country. In New York City, a pharmacist who we occasionally use, Mrs. Becker went in to make an enquiry the other day at my request to find out whether it is available, and he said, "Yes, on a prescription; $22 for 2 ounces."

Now, I have a friend of mine who lives in Seattle who travels to Oregon as a salesman. I asked him to pick some up for me in Portland, where certainly, where it is legal, it ought to be very cheap. He sent me a small bottle marked prominently as being 50-percent water, and that was $13.75.

Now, I understand that the compound itself can be manufactured at practically nominal cost, and as result of it, there is this firm—apparently, all the bottles I have seen that have not come from Dr. Jacob have come from some outfit in Salt Lake City, and they are getting outrageous prices for this product.

Senator KENNEDY. Yes, Ms. Roberts?

Ms. ROBERTS. Yesterday, we received from Nevada—it is a United States holding company; they will mail orders—they have sent me some DMSO, a pint for $30, a quart for $55. I can get that mail order. So if I do not get it anywhere else, I will drink it industrial, by the way; I drink it.

Mrs. PUCCIO. Senator Kennedy?

Senator KENNEDY. Yes.

Mrs. PUCCIO. In the magazine "Spotlight," they have an article that DMSO can be purchased in Tijuana, Mexico for $20. I have some DMSO, if you would like to see it.

Senator KENNEDY. We will consider that a little later in the hearing.

I want to thank all of you very much for your presence here.

Daryle, how long did those huddles last when you had some of your——

Mr. LAMONICA. When you are the quarterback, you can call those very quickly; you got in and got out real quick, especially when I was using it.

The strange part about it, you cannot realize the smell because you take it yourself. You can in your taste; foods taste pretty much all the same. But to the ladies here that have used it, there is no odor. But Mr. Potter, when we got in the elevator, I knew somebody was using DMSO.

Ms. ROBERTS. Excuse me. I am very proud of the odor. [Laughter.]

Senator KENNEDY. Is Oakland going to go to L.A. or not, Daryle?

Mr. LAMONICA. Well, we are going to stay in Oakland this year.

Senator KENNEDY. OK. I want to thank you all, unless my colleague——

Senator METZENBAUM. No; that is fine.

Senator KENNEDY. Thank you all very much for your presence here; it has been very helpful.

We will be in order now.

Dr. Jere Goyan, who is the Commissioner of the Food and Drug Administration, will be our next witness. Due to the nature of the hearing, we do have some conflicting testimony, we are going to follow the procedures of the committee, and I am going to at this time swear in the panel. I will ask you if you will all rise and stand with me.

Do you swear the testimony you will give is the truth, the whole truth, and nothing but the truth, so help you God?

Dr. GOYAN. I do.

Ms. BUC. I do.

Dr. HENSLEY. I do.

Dr. CROUT. I do.

Dr. PANI. I do.

Senator KENNEDY. Let the record show that all of the witnesses responded affirmatively.

Commissioner, do you want to introduce your panel here?

STATEMENT OF JERE E. GOYAN, COMMISSIONER, FOOD AND DRUG ADMINISTRATION, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES; ACCOMPANIED BY NANCY L. BUC, CHIEF COUNSEL, FOOD AND DRUG ADMINISTRATION; MICHAEL J. HENSLEY, DIVISION OF SCIENTIFIC INVESTIGATIONS, BUREAU OF DRUGS, FOOD AND DRUG ADMINISTRATION; J. RICHARD CROUT, DIRECTOR, BUREAU OF DRUGS, FOOD AND DRUG ADMINISTRATION; AND K. C. PANI, DIVISION OF ANTI-INFECTIVE DRUG PRODU[illegible] BUREAU OF DRUGS, FOOD AND DRUG ADMINISTRATION

Dr. GOYAN. Yes, thank you, Senator. On my left is Ms. Nancy L. Buc, Chief Counsel of the Food and Drug Administration; on my immediate right is Dr. Michael J. Hensley, Division of Scientific Investigations of the Bureau of Drugs; to his right is Dr. Richard J. Crout, Director of the Bureau of Drugs; and to Dr. Crout's right is Dr. K. C. Pani from the Division of Anti-Infective Drug Products of the Bureau of Drugs.

Senator, I am pleased to be able to join you here this morning to discuss the drug DMSO. Like millions of other Americans, I have long been concerned about the lack of good drugs for use in chronic, debilitating diseases such as arthritis, and therefore, in the early 1960's, I was excited by the potential of DMSO as a drug for use in these types of diseases. However, in the years that passed after that, I noted that like so many drugs that are put forward as possible wonder drugs, it seemed to fade and disappear.

After joining the Food and Drug Administration several months ago, I became aware of the fact that there was great continuing interest in the drug. I also, of course, became aware of the fact that the Federal Food, Drug, and Cosmetic Act requires that a drug be proven both safe and effective before it can be made available to the American people. This is a good law. It is one that prevents

people from preying on the ill by offering cures which are not really cures.

However, at the request of a Congressman, I personally reviewed the scleroderma report of the Arthritis Advisory Committee of the Bureau of Drugs to look and see whether or not I agreed with the decision that had been made by the Bureau. Reluctantly, I was forced to agree that the efficacy of the drug had not been proven, although it did show promise.

Because of that interest, I continued to look into it further, and was disappointed to note that most of the investigational new drug protocols which I looked at were dealing with uncontrolled experiments, or what we would call primarily anecdotal-type approaches. Thus, I was concerned that it would be highly unlikely that most of those protocols would result in providing any definitive answers about either the safety or the efficacy of the drug.

More recently, it has been brought to my attention that our biological monitoring program, what we usually refer to as our BiMO program, had been turning up some disturbing findings relative to several of the clinical investigators and sponsors and monitors of this particular drug and its studies. These findings alleged that the clinical investigators, or perhaps in some cases the sponsors, had not followed their original scientific protocols, had not reported some of the side effects that had been found by the investigators, and that in some cases they may even have chosen to report only the favorable data. That was, of course, very disturbing.

It was also reported to me at the same time that strong differences of opinion had arisen between the Bureau management and the Division of Scientific Investigations as to the proper way of following up on the original findings. Now, I must hasten to say that it is not unusual for there to be differences of opinion between our investigative people and management in the Bureau or in any of the other bureaus. This arises because of the fact that the investigators are always looking very specifically at a given case and they want to go take care of that; on the other hand, management has to look at the total picture and consider all possibilities.

Nevertheless, this concerned me, and I asked Ms. Buc, our chief counsel, and Mr. Paul Hile, who is our Associate Commissioner for Regulatory Affairs, to look into the management of the investigation. Shortly after that, the Inspector General asked us to stop that investigation because of an investigation that he had begun. However, the interest on the part of the Office of the Commissioner led to the formation of a steering committee which now oversees all of our efforts on DMSO investigations. However, when the Inspector General completes his investigation, we will then continue ours and assure ourselves that we are pleased with the outcomes.

Senator KENNEDY. Is the U.S. attorney in Baltimore involved?

Dr. GOYAN. Yes, sir.

Senator KENNEDY. Is that usual, or is that unusual?

Dr. GOYAN. It certainly is unusual, yes, sir.

Senator KENNEDY. Why would he be involved?

Dr. GOYAN. He was involved, I believe, because of the fact that it had been brought to the attention of the Inspector General, who in turn consulted with the Baltimore U.S. attorney in regard to possible malfeasance on the part of some employees of the agency.

Senator KENNEDY. Is there anything that we should know about that, about malfeasance?

Dr. GOYAN. Well, the problem I have with that, Senator, is that the Inspector General has told us that we cannot look into it further, and until I get a report from him, I really know no further about it.

Senator KENNEDY. All right.

Senator METZENBAUM. Doctor, malfeasance would not necessarily be a criminal act, so I am trying to get the tie as to what the U.S. attorney is looking into.

Senator HATCH. Malfeasance which way?

Dr. GOYAN. I am sorry, Senator. As a nonattorney, I sometimes misuse those sorts of terms. Perhaps our chief counsel could enlighten us on it.

Senator METZENBAUM. I am just trying to get the concept; I am not trying to prejudge the issue. I would like to understand what is involved. Could your counsel advise us?

Ms. BUC. As the Commissioner said, we have a relatively limited amount of information as to what they are looking into, much less what they found. As I understand it, the allegations have to do with the question of whether the sponsor and the investigators were investigated promptly enough and in a proper fashion, and also may have to do with questions that pertain to the sponsor and to the investigators. But that is almost literally all we know; they have been most closemouthed about what they are investigating.

Senator KENNEDY. I guess we will come back with Dr. Hensley. He is going to comment on some of these matters a little later.

Dr. GOYAN. In any case, Senator, these questions that were raised by the BiMO investigation and by the lack of well-designed studies make it necessary for me to report to you today that we still do not know the answer to the question of whether or not DMSO is or may become a useful therapeutic agent.

As an agency, we are bound to find ourselves constantly accosted, as you well know, by those who want to declare a drug a success on the basis of a few testimonials. But the Congress, in its wisdom, in the past has insisted that any drug that does not work is not truly safe and that the public deserves protection from drugs that do not work and are likely to be just cruel hoaxes.

It is certainly my hope that several studies now underway on scleroderma, spinal cord injuries, and others, will result in definitive answers in the relatively near future as to DMSO's place in the spectrum between quackery and a useful and important drug.

Thank you very much.

Senator KENNEDY. Dr. Hensley, DMSO is currently approved on the market for use in one condition, is that correct?

Dr. HENSLEY. That is correct.

Senator KENNEDY. And what is that?

Dr. HENSLEY. Interstitial cystitis; it is a form of——

Senator KENNEDY. Do you want to repeat that?

Dr. HENSLEY. Interstitial cystitis; it is a form of bladder inflammation.

Senator KENNEDY. A form of what kind of inflammation?

Dr. HENSLEY. Inflammation of the urinary bladder; unknown cause, I think.

Senator KENNEDY. Now, that approval was based on two studies, as I understand it; one by Dr. Shirley and one by Dr. Stewart, is that correct?

Dr. HENSLEY. That is correct. The data submitted for Dr. Shirley was a 51-patient study; the data submitted for Dr. Stewart was a 15-patient study.

Senator METZEMBAUM. I am having difficulty hearing the witness. Could you speak up a little, please?

Dr. HENSLEY. Yes. What I said was that there were two studies: one by Dr. Shirley, which was a 51-patient study; the second by Dr. Stewart, which was a 15-patient study.

Senator KENNEDY. Now, subsequent to the approval of the DMSO, a routine inspection was carried out of Dr. Shirley, is that correct?

Dr. HENSLEY. That is correct.

Senator KENNEDY. What were the results of that inspection?

Dr. HENSLEY. That routine inspection was a part of the bioresearch monitoring program, wherein we visited the sponsor, Research Industries, to see what kind of monitoring they were doing at the time, and then checked with two of their clinical investigators, randomly chosen, to see how the monitoring that was conducted actually stood up.

We visited Dr. Shirley and Dr. Stewart both. The Shirley inspection was disturbing, in that although Dr. Shirley had been given 10 days' notice, he had difficulty producing the background information, the raw data that would support the safety claims that were made.

Senator KENNEDY. All right. And did that lead to a subsequent inspection?

Dr. HENSLEY. Yes, it did; it led to one of our so-called "for-cause" inspections. This inspection was designed to compare case report forms—I believe 15 were chosen randomly—to the patient records, and if the underlying data that had previously been missing was still missing, the intent was also to pursue beyond that; to go, in fact, to the laboratories who had allegedly done that data and, if necessary, to the patients.

Senator KENNEDY. What were the kinds of problems they were running into, deficiencies?

Dr. HENSLEY. From our point of view, virtually every possible deficiency; for example, there were no records of consent. Where appropriate and where necessary, institutional review board approval did not appear to have been obtained. More important, I guess, there were problems with the data.

Senator KENNEDY. With the data?

Dr. HENSLEY. With the data.

Senator KENNEDY. What sort of problems?

Dr. HENSLEY. Well, I guess we should probably talk about the safety data and the efficacy data, because they really should be separated out.

The safety data would be the ophthalmologic exams, the eye exams, that were supposed to be done before the study and minimally every 3 months during the study and subsequent to the study; and the laboratory work, a battery of tests to be done before the study and on a monthly basis during the study and after the

study. That safety data, a good part of it, we could not validate or verify because the underlying records were not present.

We did pursue that, or our investigators did pursue that and were unable to confirm that the work had been performed. Patients were interviewed, and it did appear from the interviews that we had that most of the patients had not had the lab work or the eye exams as they had been reported to have had. The case report forms that we had inhouse showed that all of this work had been done and that the results were normal.

The efficacy data, which is really the other half of it, was also disturbing, in that we had in the agency received two sets of case reports, at least, from Research Industries on Dr. Shirley's study; one was earlier in time, about late 1975 or early 1976, which showed generally good to excellent results, and the second had come in just a little bit later than that, a few months later, on a resubmission of the NDA, which showed some of these patients deteriorating, perhaps. The review of Dr. Shirley's records made it look a good deal worse than that, in that it appeared that many of the patients whose records we inspected, although they might have had initially a very good response, generally did deteriorate and often required other medication or surgery.

Senator KENNEDY. What is the agency's position with regard to the Shirley study?

Dr. HENSLEY. That is a good question. I think the position of the Division of Scientific Investigations is as it has been in the past; that the data simply cannot be used. With respect to the agency's position, I think I would have to defer to Dr. Goyan.

Senator KENNEDY. Pardon?

Dr. HENSLEY. I think I would have to defer to Dr. Goyan.

Senator KENNEDY. Doctor Goyan, just based on these observations, the difficulties in verifying certain information, the altered and changed data and the difficulty of locating the data—you are charged by the Congress and the law that there will be two studies that are scientifically sound for the approval of a various drug.

With this kind of information that has been developed by Dr. Hensley, how would you characterize the Shirley study itself?

Dr. GOYAN. Well, certainly, we would have to characterize the Shirley study as unsatisfactory. However, we are also looking at the other study that was done, and after we have completed these, then we will have to make a decision as to whether or not we should move to a notice of hearing and further action.

Senator SCHWEIKER. How many studies are in question now? How many studies are we talking about?

Senator KENNEDY. There is the Shirley and the Stewart studies.

Senator SCHWEIKER. Is that all?

Dr. HENSLEY. No, I am afraid not.

Senator SCHWEIKER. How many are there?

Dr. HENSLEY. It is hard to classify what is and is not a study. We have done a number of inspections. Many of the doctors have done one or two patients. I do not think I would classify those as studies.

We have looked at least three other studies that run from 9 to 15 patients each, and I think all of those are equally subject to question.

Senator SCHWEIKER. So that, in addition to the two you mentioned, there are three that you are at least looking at, whether they are studies or——

Dr. HENSLEY. We have looked at a good many; yes, there are at least three others.

Senator SCHWEIKER. There are three more that are still in question?

Dr. HENSLEY. At least.

Senator SCHWEIKER. Is that an accurate interpretation?

Dr. HENSLEY. At least three. There are others for whom we have verbal reports from inspectors in the field, but have not data inhouse, so I would hesitate to make any sort of judgment until I see it.

Senator SCHWEIKER. Is there any pattern in this, or is each problem study case somewhat different?

Dr. HENSLEY. Yes, there is a general pattern. It seems to be an inclination on the part of the physicians not to do the safety work. Different reasons have been offered. And by the safety work, I mean the eye exams and the laboratory work.

There also is an inclination to, I think, overlook or maybe not see or maybe deliberately ignore—and I do not know how to characterize it—possible adverse effects or possible—well, just possible adverse effects; I guess that is the best way to characterize it.

Senator KENNEDY. You conducted an investigation in the Stewart study, did you not?

Dr. HENSLEY. As part of that original routine inspection of Research Industries, a followup inspection of Dr. Stewart's study was done.

Senator KENNEDY. Could you describe what you found in that case?

Dr. HENSLEY. An audit of that 15-patient study was, while not entirely clean from the regulatory point of view, I thought, was generally good. He generally seemed to be in compliance with the regulations. The data that was looked at seemed to be supported by the patient records.

Senator KENNEDY. Was there any further information that you found out about the Stewart study?

Dr. HENSLEY. Yes; we have had some additional information on that. The original NDA was twice submitted to the agency; the last time, I believe, in 1976, and finally approved in 1978. In September 1979, for reasons I expect we will get into later, another package of data was submitted to the agency by Research Industries. This package of data contained not 15 patients of Dr. Stewart, but 40.

We have looked at that data, and it is apparent that a good many of those patient reports had been available prior to the NDA submission and were contemporary with Dr. Stewart's other patients. It appeared, therefore, that a selective submission of data had been made to the original NDA.

Now, if you look at those case report forms, they seem to have certain things in common. Many of the patients are patients who were seen at the Cleveland Clinic by Dr. Stewart perhaps once or twice, treated with DMSO, and then he apparently provided DMSO to other physicians in other parts of Ohio or, in fact, other parts of the United States, who then followed up on the patient. Many of

the patients—in fact, I guess the majority of those that are truly interstitial cystitis—had either fair or poor responses to the treatment.

Senator KENNEDY. Is that usual that you would have——

Dr. HENSLEY. A partial submission?

Senator KENNEDY. Partial submissions.

Dr. HENSLEY. I would not think so. The Federal Food, Drug, and Cosmetic Act requires full submissions. It should not have been——

Senator KENNEDY. So there have been questions raised about both of the studies that were the basis for the approval?

Dr. HENSLEY. Yes.

Senator KENNEDY. Now, was any other data reviewed with regard to the use of DMSO for its approved condition?

Dr. HENSLEY. Yes; as I indicated, that September 1979 submission by Research Industries of additional data was looked at. I looked at it first, I suppose, in February of this year; it had been in the reviewing division. It occurred to me at the time that since this material seemed to be designed to replace the Shirley data, and because of the nature of the case reports that I was looking at, that probably we ought to do some additional investigations. We did send out a number of routine assignments on that package of information.

Because of the results of some of those inspections, we subsequently sent out other assignments on other investigators whose data had not been reported to us.

Senator KENNEDY. During the course of the overall review of DMSO, you went back and reviewed the FDA's original NDA review conducted by Dr. Pani.

Dr. HENSLEY. That is correct.

Senator KENNEDY. That had been the basis for the approval of the drug in 1978, is that correct?

Dr. HENSLEY. That is correct.

Senator KENNEDY. What did you find out and conclude when you did that?

Dr. HENSLEY. As to the receipt of the initial routine report on Dr. Shirley and Research Industries and Dr. Stewart back in 1978, it occurred to me that we probably ought to do that "for cause" on Dr. Shirley's study, and as a part of that, I went back and reviewed all of the data in the NDA.

As I mentioned before, there were obviously at least two submissions: One, an earlier submission that generally showed excellent responses; and the second, a later submission that showed many of these patients perhaps not doing quite as well.

It was apparent to me that the medical officer review was based on the initial submission rather than on the second submission, and because of that appearance, I raised the issue with Bureau management as a part of our presentation of the Shirley case.

Senator KENNEDY. Now, as I understand it, as part of the widening DMSO investigation, you conducted an inspection of the Research Industries and also conducted an inspection of some of the other studies being conducted under another NDA. One of those studies was the study of Dr. Scherbel.

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What did the inspection of Dr. Scherbel turn up that was of unusual significance with respect to the possible toxicity of DMSO in humans?

Dr. HENSLEY. As you have noted, we have done a number of other inspections, and these included that September 1979 submission and also the pivotal studies that had been submitted for the scleroderma NDA; Dr. Scherbel's was one of those.

We did not inspect, however, the NDA submission. What we were looking at was another study that he had done that we happened to have picked up. It was an oral study—I am sorry—a study of the use of DMSO orally in scleroderma. That study had been listed as one that Dr. Scherbel intended to do in IND 13097, which was specifically for that indication. That IND had been submitted to the agency December 28, 1976. An inspection of Dr. Scherbel's study showed that 9 of the 11 patients on the study had been started on the oral DMSO well before the IND was submitted.

The problems with the study are generally not so much regulatory, but what the data showed, and the data showed that a number of the patients—in fact, all of the patients to some extent or another—had developed ocular problems while on DMSO. Now, in fairness, some of those patients had had ocular problems prior to DMSO treatment. These eye problems were, according to the report we received initially, identical to those seen in the animal studies in 1966 through 1970.

Senator KENNEDY. When was that reported?

Dr. HENSLEY. To the agency?

Senator KENNEDY. Yes.

Dr. HENSLEY. It was not officially reported, as far as we can tell. We, as I said, picked up on this during an inspection, during a routine inspection of Dr. Scherbel; we went back on this "for cause" that I have mentioned. We got the report of the inspection, the initial one, in April of this year, April 22, 1980.

Senator KENNEDY. What is the significance of the finding?

Dr. HENSLEY. Well, the significance to me was that, I guess, on April 22, 1980, I was standing there with an inspection report in my hand of an oral DMSO study, a study wherein patients had been given doses very nearly approaching the animal studies that had showed ocular toxicity, and it appeared from the material that we had discovered during this very first, initial tipoff inspection that the eye changes that were being reported in these patients were identical to those seen in the animal studies back in the sixties. The significance, I think, is obvious.

Senator KENNEDY. Well, now, is it not fair to say that all along in the use of DMSO, people were looking for possible human eye toxicity, because it had been shown to be toxic to the eye in animal studies; is that not right?

Dr. HENSLEY. People were aware of it, and we assume people were looking; yes.

Senator KENNEDY. The Scherbel report was the first evidence that there might possibly be that problem with human eyes?

Dr. HENSLEY. That is correct.

Senator KENNEDY. Therefore, it had some extraordinary significance, did it not?

Dr. HENSLEY. Yes, it did.

Senator KENNEDY. When was the actual date that the Scherbel report was written?

Dr. HENSLEY. It turns out that the initial report of the oral scleroderma patients had been noted by Dr. Scherbel to Research Industries on May 4, 1977.

Senator KENNEDY. What other letters did you find relevant to the May 4 letter?

Dr. HENSLEY. Subsequent to the "for-cause" inspection of Dr. Scherbel that disclosed the extent of the eye problem, we did issue an assignment to inspect Research Industries. In fact, we have twice inspected the firm in this regard and have discovered correspondence that indicates that the Scherbel report was received; that, in fact, there is a letter, which I believe is dated May 17, 1977, from Mr. Moyle, who is president of Research Industries, to Dr. Scherbel which appears to indicate that Dr. Jacob informed Dr. Pani at FDA verbally of that finding, and that subsequently, or perhaps at the same time, as we have learned from another letter, the Scherbel report may have been provided to FDA.

This exchange of correspondence and these letters that you are referring to are of great importance to me, personally, in my particular line of work. It appeared that Research Industries had had reported to them a possible adverse effect in 1977, and yet had never reported it to the agency because, in our files, we found none of these reports.

I believe that Dr. Pani was interviewed, and denied he had ever been told any of this. We therefore had the possibility of a violation of the Federal Food, Drug, and Cosmetic Act, and also, perhaps, of title 18, section 1001—the making of false reports to the Government.

The reason we were concerned about that particular statute was that a number of reports had come in since 1977 disclaiming eye lesions in humans secondary to DMSO or associated with DMSO.

Senator KENNEDY. Mr. Commissioner, how serious would that be—the failure to have that kind of a report available to the agency itself? How serious is that?

Dr. GOYAN. I would consider that extremely serious, Senator, especially in view of the fact that it was the toxicity that we were most concerned about.

Dr. HENSLEY. May I add something?

Senator KENNEDY. Yes.

Dr. HENSLEY. I just wanted to note that our regulations under which we work provide that the sponsor shall promptly investigate any report to the Food and Drug Administration and to all investigators any findings associated with the use of a drug that may suggest significant hazards, contraindications, side effects and precautions pertinent to the safety of the drug. That is the situation we thought we had.

Senator KENNEDY. Certainly, the kind of side effects that you are talking about here fall clearly within that definition.

Dr. HENSLEY. Yes, and it made the examination earlier in 1978 of Dr. Shirley's study that much more significant because, as you will see if you examine the records of the agency, we had a limited number of patients reported to us by Research Industries. We had

51 from Dr. Shirley, and it appeared that perhaps those eye exams had not been done.

We had 15 by Dr. Stewart. We had another NDA on scleroderma which contained no more than that total number of patients. So, it looked as though perhaps a good many of the investigators had not been looking for eye changes, and when they had looked, they had found some.

Senator KENNEDY. So it appeared from these four letters that this was the first report of human eye toxicity and that the company had furnished it to Dr. Pani at FDA.

Dr. HENSLEY. That was the appearance of the letters, yes.

Senator KENNEDY. According to the letters?

Dr. HENSLEY. That is correct.

Senator KENNEDY. But when you went back, you did not find any; is that correct?

Dr. HENSLEY. Went back to FDA, you mean?

Senator KENNEDY. Yes.

Dr. HENSLEY. Yes. They looked internally, as I understand it, and they were not found.

Senator KENNEDY. They were not found?

Dr. HENSLEY. That is correct.

Senator KENNEDY. Did you also find that Dr. Scherbel was using DMSO or other types of drugs for which there was no IND?

Dr. HENSLEY. Yes. The other problem, which I guess does fall under the regulatory classification—the one regulatory problem that I guess we do have with Dr. Scherbel is that we found two drugs—87-2, which is DMSO plus urea, and another called Satori, which is dimethyl sulfon—that apparently had been dispensed to a few of his patients. He stated he had received these drugs from Dr. Jacob.

We searched the records at FDA. There was no record of an IND for either of these drugs.

Senator KENNEDY. What action did your division propose?

Dr. HENSLEY. Well, at this time, as I said, it looked as though we might have violations of the Federal Food, Drug, and Cosmetic Act and perhaps of title 18. And there was the thought that perhaps there was some conspiracy to conceal this information. I am trying to give you our thoughts at the time, not necessarily what the case may be.

We also had the appearance that at least some of this data might have been reported to someone in the agency. I do not have the jurisdiction to investigate within FDA, and I do not think our division does.

We felt at the time that two courses of action were appropriate. One, additional followup investigations needed to be done by clinical investigators, at Dr. Jacob's facility, and at Research Industries.

Two, we felt that in fairness to Dr. Pani, rather than subjecting him to any sort of informal or unfair type of interview or interrogation, we ought to refer the matter to our FDA internal policy management people so that they could investigate the situation, and we made a recommendation to that effect on the 5th of May.

Senator KENNEDY. Was that action implemented?

Dr. HENSLEY. In a sense. The action was implemented in a stepwise fashion, with some of the steps being omitted, you might say.

We approached the Bureau of Management on May 5, as I said, with our plan. It was felt, as I perceived it, that perhaps policy management should not be involved. In fact, we were prohibited from referring the matter to policy management. I believe that Dr. Kelsey had also suggested referral to the Inspector General; that, too, was prohibited.

Subsequently, apparently because of the political sensitivity of DMSO, a restraint, you might say, was placed on our efforts to investigate the matter, in that all proposed inspections, I think, from the 7th of May onward had to be routed through the Bureau of Drugs Management for clearance. That involved going through three or four levels of people for clearance.

Senator KENNEDY. Does this mean that you were prohibited from bringing it up to your Inspector General?

Dr. HENSLEY. Yes, prohibited from going to the Inspector General.

Senator KENNEDY. You were restrained from bringing it up from the time of May——

Dr. HENSLEY. May 7 is when the controversy on this sort of reached its peak.

Senator KENNEDY. What reasons were given to you for that?

Dr. HENSLEY. Essentially, the political sensitivity of DMSO; I think there was a great reluctance to challenge Dr. Jacob because of his political clout, if you will. I do not really think there were any other issues at that time.

Senator KENNEDY. What did you and your colleagues in your division feel about the instructions?

Dr. HENSLEY. We were concerned from a number of points of view. First of all, we were concerned from the point of view of public health, in that it appeared that we might have a health problem—specifically, eye toxicity from DMSO in humans.

It also appeared that two investigational drugs, 87-2 and Satori, for which there was no IND and, to my knowledge, no animal testing, might be distributed in interstate commerce and might be used by the general public.

Another concern that we had was simply our job, if you will; we perceived that there were possible violations of the Federal Food, Drug, and Cosmetic Act and title 18 and we wanted to investigate them. We perceived that there might be a conspiracy in that there was some reason for haste in this. We felt that it was necessary to move expeditiously.

I think, finally, there was a concern on our part as to whether or not the instructions to not to go to the Inspector General, or not to go to policy management were, indeed, legal orders—we were concerned that they might be, in fact, illegal orders. So we did, as I think you know, made a couple of consultations.

One, we consulted with a representative of general counsel at FDA. My supervisor, Dr. Lisook, did that; that was in that same week, I think, around the 8th or 9th of May. Two, I contacted a friend of mine who works——

Senator KENNEDY. What did the general counsel say?

Dr. HENSLEY. He indicated that, yes, that was an illegal order; it was improper; we should go directly to policy management with the issue.

I also contacted a friend of mine who works for the Office of Inspector General, and without giving him any details whatsoever of the case, proposed to him in general terms what we were faced with, asking his advice. I told him, "Listen, I do not know what obstruction of justice is; I do not know what is or is not proper in this case; I have never been in this kind of a situation. If I obey these orders, if I do not go to policy management and if I do not go to Inspector General and come to you in an official way and make an official complaint, and if I do not pursue these investigations aggressively, where we seem to have the possibility of criminal violation, am I legally liable? Is my supervisor, Dr. Lisook, legally liable; is Dr. Kelsey legally liable? Are we guilty of obstruction of justice?"

The answer was, "Yes, you probably are." I was asked to speak then with one of the supervisors with the Office of Inspector General, and I said I would do so but only on an informal basis and I did not intend at that time to make a complaint because I felt that we could work it out within the agency. I felt that this was probably a little bit of over-reaction and that indeed it was a politically sensitive issue.

So I asked for 3 or 4 days' time; in fact, I specified a date. I said, "Listen, if we do not get authorization to proceed by this date, I will give you all the information."

I did meet with the Office of Inspector General representative the following day. He also informed me that, yes, I was up to my neck in it and if I played along, I would be legally liable. I did hold to that contention, though, that I wanted to take a few more days, and I said I would take my chances with the press. The press happened to get a leak over the weekend, and we were talking on a Friday. I realized then that I would be in some hot water.

At any rate, the Tuesday came that I had set. The clearance was given by bureau management to proceed at least on one aspect of the investigation. The Office of Inspector General people, however, decided that they wanted to proceed with their investigation, and they did, and I was then questioned extensively, as were other people.

Senator KENNEDY. So this is how the U.S. Attorney became involved?

Dr. HENSLEY. That is correct. The Office of Inspector General, I think, went to the U.S. attorney in Baltimore, because it is the judicial district, and briefed them on what they knew of it. They obviously interviewed a great many people during that week and had some very definite impressions as to what they ought to do.

Senator KENNEDY. So what action has the FDA subsequently taken or not taken?

Dr. HENSLEY. Subsequently, as the Commissioner indicated, a task force has been set up to coordinate the investigation. We have, on our part, attempted, as I said earlier and described earlier, to expand the investigations that we had intended to do on the clinical investigators. We have attempted to get a better handle on the DMSO data both on scleroderma and on interstitial cystitis.

We proposed, I guess, initially a set of 17 investigations on the 19th of June. Now, eventually, I think, on the 10th of July, those

investigations were approved and, in fact, most of them have been done since. Once they were approved, they were done expeditiously.

An investigation of Dr. Jacob and the business of the 87-2 and Satori, and an investigation of the matters that have been disclosed by these 17 investigations, together with a few others that were put together, have not yet occurred, however.

Senator KENNEDY. Let me ask you, Mr. Commissioner, about how you would characterize the scientific work that has been done and submitted to the FDA on DMSO.

Dr. GOYAN. I think, in general, it has not been of high quality.

Senator KENNEDY. How serious, from a regulatory point of view, are the kinds of deficiencies that were found in the Shirley study, which has been used, in part, as the basis of approval for DMSO?

Dr. GOYAN. Those are extremely serious.

Senator KENNEDY. How serious is the failure to report the eye problems in the human subjects? I think you referred to that a little bit earlier.

Dr. GOYAN. Yes. I indicated earlier that I would consider those among the most serious because of the fact that that was a side effect we had anticipated from the animal studies.

Senator KENNEDY. What if it was reported and not acted upon by the medical office; how serious is that?

Dr. GOYAN. Senator, I would consider that serious enough to believe that the individual responsible should be removed from the agency.

Senator KENNEDY. Well, why has the agency not inspected Dr. Jacob?

Dr. GOYAN. Well, when we issued orders to the Seattle district office to inspect Dr. Jacob, they called, which is standard procedure, and Dr. Jacob indicated he would not allow them to inspect him. They reported that back to us and asked for additional orders with regard to how we would go about it and what we were looking for, et cetera. We have, in the meantime, attempted to determine exactly how we should go about this, in the belief that we would probably have to develop an administrative warrant. In order to get such a warrant, it was our belief that we needed a strong case, and consequently that it would be worthwhile to visit some of the other clinical investigators and see if there was additional information that would strengthen our case for an administrative warrant.

Senator KENNEDY. Well, do you intend to inspect Dr. Jacob?

Dr. GOYAN. Yes, we agreed to do that as of yesterday.

Senator KENNEDY. As of when?

Dr. GOYAN. Yesterday. The steering committee met yesterday and went over the plan and we have agreed to the inspection.

Senator KENNEDY. How can things sort of develop into such a state within the Food and Drug Administration? We know that one group of people—in this case, the investigators—feel that another group of people—in that case, the Bureau of Drugs—has been blocking their efforts to find out the truth about the deficiencies in the DMSO studies.

How does it come to the point where you get the Inspector General or the U.S. attorney involved in investigating the internal practices of the FDA?

Dr. GOYAN. Senator, that is indeed a difficult question. Basically, as you know, I have instituted my own investigation in order to try and get at the causes. As of the moment, I cannot speak much further on it, but I am very concerned about it.

Senator KENNEDY. Did the agency investigate Dr. Pani?

Dr. GOYAN. I believe the agency did previously, not at this time.

Senator KENNEDY. And what were the results?

Dr. GOYAN. At that time, Dr. Pani was taken off of the team responsible for review of new drug applications on DMSO.

Senator KENNEDY. Why was he taken off?

Dr. GOYAN. Well, there were questions of possible improprieties in his interactions with Research Industries Corp.

Senator KENNEDY. He was left alone for 10 years with the responsibility of the review of DMSO, is that right?

Dr. GOYAN. That is correct.

Senator KENNEDY. Does that make any sense to you?

Dr. GOYAN. Well, it is hard for me to look back on it retrospectively and know. However, bear in mind that there were not a lot of studies going on in that area at the time.

Senator KENNEDY. Dr. Pani, you were the medical officer with the primary responsibility for DMSO, is that correct?

Dr. PANI. Yes, I was assigned DMSO when I came on board at FDA in 1968.

Senator KENNEDY. When was the first animal evidence developed that DMSO might have eye toxicity?

Dr. PANI. Well, it was developed much earlier. In 1963, studies came to a halt, and when I came on board, restricted studies were on the way.

Senator KENNEDY. Was the eye toxicity in animals study perceived to be a potentially serious problem for humans?

Dr. PANI. Yes. Biologically, I think that eye toxicity in humans has to be looked for very carefully. I think we did present in a Federal Register statement on September 10, 1968, the guidelines for conducting clinical studies with emphasis on eye examination.

Senator KENNEDY. Did they take any action in the FDA in the time 1965–1966?

Dr. PANI. Action was taken as soon as the evidence of eye toxicity was revealed in animals. The studies in humans were halted and the clinical records were reviewed. When the eye problem was brought to light, since the physicians were treating incurable diseases, the agency was giving permission for DMSO use, on a case-by-case, investigator-by-investigator basis, asking them to follow the guidelines of the Federal Register statement of September 10, 1968, or thereafter.

Senator KENNEDY. Is it fair to say that the primary problem everyone was looking for was eye toxicity, following 1965?

Dr. PANI. Yes, Senator. The FDA has very strict Federal guidelines. In a 14-day study, eye examination is not required at dose levels of 1 gram per kilogram body weight for topical application. On the other hand, for a chronic topical study, a complete eye examination has to be done prior, during, and after treatment, including slit lamp examination. If any adverse reaction occurs, the sponsor of the investigations is required to notify the agency.

Senator KENNEDY. When did you learn of Dr. Scherbel's work which indicated a potential problem of eye toxicity in human beings?

Dr. PANI. The first time I came to know about it was, as I recall, on May 7, when we had a meeting with Mr. Frankel.

Senator KENNEDY. May 7 of when?

Dr. PANI. May 7 of 1980, when we were called to Mr. Robert Frankel's office; he is Deputy Associate Director for New Drug Evaluation. At that time, I was accompanied by Dr. Gibson, who is the director of our division. At that time, Mr. Frankel showed me a letter of May 4, written by Dr. Arthur Scherbel to Mr. Henry Moyle, sponsor.

Senator KENNEDY. What year is that?

Dr. PANI. May 4, 1977.

Senator KENNEDY. So you saw the May 1977 letter in May of 1980?

Dr. PANI. Yes, sir.

Senator KENNEDY. Do you mean it is your testimony that that was never brought to your attention?

Dr. PANI. No.

Senator KENNEDY. It never was brought to your attention?

Dr. PANI. I had never seen it. That was the first time that Dr. Gibson and I saw that letter.

Senator KENNEDY. Had it been brought to your attention, what would you have done?

Dr. PANI. I would have reacted immediately. Since we were looking for the eye problem all along in the DMSO study, it would have been like spotting a wolf in the midst of a herd of sheep. I would have immediately halted the study and demanded a thorough followup.

Senator KENNEDY. Do you have any idea about why that amount of time would pass and you would not get that kind of information?

Dr. PANI. Followup data were never submitted; neither the IND records nor the NDA records show that they were submitted.

Senator KENNEDY. So your position is that the company never reported it?

Dr. PANI. No, they never reported it.

Senator KENNEDY. They never reported it to you or to——

Dr. PANI. No, we do not have any such documents in our possession.

Senator KENNEDY. Dr. Pani, the policy management staff at the FDA conducted an investigation of you and your relationship with the sponsors, the monitor and clinical investigators of DMSO. The Commissioner has described the actions that were taken as a result of that investigation. Do you wish to respond in any way?

[Pause.]

Dr. PANI. May I have the question again, sir?

Senator KENNEDY. There have been some comments here earlier about your work and about your association with the company and the sponsors of the drug itself. The Commissioner has described, also, the actions that were taken as a result of the investigation of the work for which you had responsibility and I just wanted to give you an opportunity to make any comments or rebuttal of some of the statements or comments that were made here this morning.

You were transferred off the drug, and I want to make sure that you have a full opportunity to express whatever view that you have.

Dr. PANI. From 1968 on, I was assigned to handle all clinical studies of DMSO by myself. Of course, the division director is in charge, and we go by his decisions in the meetings. In 1972, FDA asked the National Academy of Sciences to evaluate all DMSO data. In 1973, we got their analysis and we have since been following their guidelines.

I also have had internal consultations on other studies that I am not familiar with; Dr. Harter and others were assigned. All this is on record.

So it is not that I am doing the whole project myself, but that a group of scientific and medical people in our agency were jointly developing the protocols, and evaluating results, and I was coordinating these efforts.

Senator KENNEDY. Well, Mr. Commissioner, what kind of potential legal action must FDA contemplate against various parties as a result of the DMSO fiasco?

Dr. GOYAN. I will leave that to my chief counsel.

Ms. BUC. There are a series of actions that will have to be considered. Any of the clinical investigators who have violated our regulations will have to be considered for potential disqualification as clinical investigators, and that is a process that is begun by the Bureau of Drugs. They are entitled to a hearing, and it ultimately reaches the Commissioner.

In addition, to the extent that the information that the Inspector General or any of us turn up results in allegations of criminal activity, I know that we will be considering criminal prosecution as well, for the investigators, if there are allegations of criminality there, and, if it comes to that, the people at the agency as well.

Senator KENNEDY. Mr. Commissioner, how many people in the country, in your best estimate, use DMSO every year?

Dr. GOYAN. I would guess, Senator, that it may be as high as in the hundreds of thousands.

Senator KENNEDY. How many?

Dr. GOYAN. Perhaps into the hundreds of thousands.

Senator KENNEDY. Does that include people who go outside the country and go down to Mexico?

Dr. GOYAN. Yes.

Senator KENNEDY. Has it been increasing?

Dr. GOYAN. I have no doubt that it has been increasing since early March, when television did a piece on DMSO.

Senator KENNEDY. You have heard the witnesses this morning describe taking DMSO orally and intravenously. You have heard them describe taking drugs related to DMSO, for which there are no IND's or NDA's. What is your reaction to that?

Dr. GOYAN. Well, all of those concern me, Senator, particularly the intravenous and oral dose forms because of the fact that you are going to get much higher doses of the DMSO internally. We know that it is in the cases where they get high doses internally that we get into the concern over possible ocular problems that were described earlier.

The fact that we could get up to the point where they are similar to the dosages that were found in animals to cause these refractory changes in the eye is very disturbing. I must also add that I would also be concerned about the unapproved drugs, because we do not know what the possible toxicities would be with them.

Senator KENNEDY. With what?

Dr. GOYAN. On the unapproved drugs.

Senator KENNEDY. They seem to be being used now as well.

Dr. GOYAN. Apparently, they must be, from your testimony.

Senator KENNEDY. Well, what would you like to say to the American people about the DMSO? We have heard some witnesses here this morning who have made a very impressive presentation.

We certainly are not experts on these matters on the Health Subcommittee. It is an issue that has been before the FDA now for 18 years. There have been studies that have been done to permit its approval. Then we find out that in the reviews of these studies, there is serious scientific information that has been lacking or distorted or misrepresented.

We find out about the enormous internal conflict within the agency itself between various bureaus. We find legal actions anticipated against a whole variety of different inspectors and researchers. We hear allegations of influence by the research company. We have allegations of conflicts of interest.

We hear your own testimony that some of these studies that point up the real danger of eye toxicity had not been brought to the attention of or acted upon by responsible officials in FDA.

It is an enormously serious situation for the agency, and potentially for the American consumer. We heard earlier from a panel of witnesses that represented a wide variety of different professions and a wide variety of different parts of the country. They spoke extremely passionately about what this drug did to help relieve their anxiety, anguish, pain, and suffering.

Now, what message do you give to the American people? One message, certainly, is that the agency itself has been caught in this confusion and bureaucratic conflict over a period of time. And you have made every indication in every statement and every comment that you are going to take the steps to deal with it. That is very reassuring; it has to be. It is reassuring for this committee and it should be for the American people. We are impressed with your resolution.

But what do you tell the American people, based upon what they hear at this morning's hearing?

Dr. GOYAN. Well, Senator, it is a very difficult thing to deal with testimonials of relief with regard to diseases that are the type for which DMSO is used. The problem is that almost all of the diseases have periods of spontaneous remission and exacerbation; that is, the patients go through times when they get better spontaneously, and times in which they get worse.

Consequently, if you happen to use the drug at a time when you are going to get better anyway, you will indeed get better. This makes any sort of testing of a drug extraordinarily difficult.

With a drug like DMSO, where using it results in a terrible garlic breath, it is difficult for people to carry out what we call

blinded studies, in which the person would rub something on that was not DMSO but did not know it was not DMSO.

So, these sorts of studies are difficult. They are possible, however, and I believe that they are underway in a number of places in the United States today and that within the next few years, we will have answers to this matter in hand.

In the meantime, I would caution the American people that the use of technical grade DMSO carries risks. We have no idea what other things are carried in the technical grade. With the unapproved drugs, we have no idea what potential toxicities may exist.

We have another side to it. DMSO is what we call a carrier. If you put something else in DMSO, it carries it right through the skin. Consequently, if you happen to have, let us say, some sort of drug on your skin and you applied DMSO to the same area, the DMSO could carry the drug through the skin and could cause other difficulties.

Therefore, I would caution the American people not to use DMSO indiscriminately. Allow us to finish up the good studies that are currently underway and find out what the answer is.

Senator KENNEDY. Well, I think the people who are listening to the witnesses here this morning—and, again, it was a rather diverse panel—an athlete, a very distinguished New York lawyer, a small businessman, housewives and professional people. They have been suffering and have had a good deal of anguish and pain, and they have taken this drug and virtually uniformly indicated that it helped them; it provided relief.

There are millions of Americans who will have listened to their testimony and who, today, are suffering and are discouraged because they cannot deal with the pain that they are facing. The treatments that they have had to date have not been satisfactory, and they listen to their fellow citizens—intelligent individuals articulate and a very powerful case.

They say to themselves, "Look, this drug has been kicking around FDA for 18 years, and we hear from these individuals that at least it is helping resolve their problems." They are wondering when they are going to get an answer. They hear of some of the tests that have recently reflected eye toxicity, and that is going to frighten them; that is going to scare them; that is going to make them really wonder.

They have to ask themselves, if the FDA is the principal agency of Government that is supposed to make the recommendation to the American people with regard to safety and with regard to efficacy, "when are we going to get an answer?"

Dr. GOYAN. Well, in fairness, Senator, remember that it is not up to our agency to promote this drug. It is up to our agency to make the decision as to whether it is safe and effective, as you pointed out.

Senator KENNEDY. Yes, but your agency is supposed to be able to tell us whether it is going to be safe and efficacious.

Dr. GOYAN. Right.

Senator KENNEDY. Well, that is the issue, I would think.

Dr. GOYAN. But the problem is that, as yet, data is not available to make that decision.

Senator KENNEDY. Yes, but we sure have to get that data.

Dr. GOYAN. I would agree with that, and I hope that the sponsor will bring it forward. But it is not up to us to make that data available, Senator.

Senator KENNEDY. It is not up to you to do what?

Dr. GOYAN. To make the data available.

Senator KENNEDY. No, but you have to give the assurance to the American people whether it is safe and efficacious, do you not?

Dr. GOYAN. But we can only do that on the basis of data that is submitted to us.

Senator KENNEDY. It is going to have to be the assurances which you give on that, on the basis of scientific information that is satisfactory.

Dr. GOYAN. Right, and I believe that we now have studies ongoing that will give us the information we need in order that we can make an informed judgment.

Senator KENNEDY. How do you think that that can best be done, and how long is that going to take to be able to do?

Dr. GOYAN. I think that that can best be done the way it is being done at the present moment, where Research Industries and one other company, Carter-Wallace, have studies ongoing with regard to a number of different uses of the drug. I believe that those are good protocols and they will be carried out correctly. From that, I think we will be able to make decisions; I would hope that it would be within 2 years.

Senator KENNEDY. Well, we have some responsibilities here too, based on the testimony at this hearing. It seems to me that it would be wise to at least invite you, the NIH, and all the manufacturers interested in producing this to a meeting, to try to least devise a process and a system and a timetable, where these issues will be resolved.

Dr. GOYAN. I would welcome that, Senator.

Senator KENNEDY. You will cooperate with us?

Dr. GOYAN. In every way.

Senator KENNEDY. Well, that is fine.

Dr. HENSLEY. Senator, may I make one other remark?

Senator KENNEDY. Yes.

Dr. HENSLEY. I think there may be a misimpression left by some of the testimony that I gave and I want to correct it.

If you look at the studies that we have surveyed by Research Industries, the bottom line is that the efficacy data that we have appears to be little more than testimonial. The safety data essentially was not done. The ophthalmologic exams that were done, when done, did not conform with the Federal Register guidelines that require slit lamp exams and changes in refractions, and those kinds of things.

So, the bottom-line answer on whether or not there is eye toxicity in humans—I think the fairest response is that it is not known at this point in time. I just wanted to make that clear.

Senator KENNEDY. Well, I think we all understand that you do not do the studies, but you can make sure that they are going to be done, or you can make sure that you get the information that you are going to need in order to give those assurances.

Dr. GOYAN. Yes.

Senator KENNEDY. That is certainly a responsibility both for the manufacturer and for the company.

Thank you very much.

Dr. GOYAN. Thank you, Senator.

[The prepared statement of Dr. Goyan follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

STATEMENT

BY

JERE E. GOYAN

COMMISSIONER

FOOD AND DRUG ADMINISTRATION

PUBLIC HEALTH SERVICE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON HEALTH AND SCIENTIFIC RESEARCH

COMMITTEE ON LABOR AND HUMAN RESOURCES

UNITED STATES SENATE

JULY 31, 1980

NOT TO BE RELEASED UNTIL DELIVERY

Mr. Chairman:

I am pleased to be here to discuss the drug, dimethyl sulfoxide (DMSO).

THE DRUG LAW

Before I discuss the issues surrounding DMSO, there is an important point that must be made in order to focus on the basic underlying issue. The hearing today illustrates well the continuing tension between pressures to speed up approval of genuine or alleged new therapies, on the one hand, and, on the other, the Food and Drug Administration's (FDA) statutory and public health obligations to approve only those drugs that have been shown by scientific evidence to be safe and effective. We are even witnessing efforts, including legislation, to bypass the scientific process entirely.

The evolution of the new drug provisions of the law is well known. Congress' message in putting these provisions into place is simple: People should be protected from unsafe and ineffective drugs; no person should accept even a small risk of injury from an ineffective drug; and no drug is safe if it is ineffective. Simple, but very meaningful. Congress provided a method of reasonably assuring the public that drugs on the market have been scientifically demonstrated to be safe and effective. And, Congress said that the burden of developing this scientific proof belongs with those who wish to market drugs.

The law containing these principles of safety and effectiveness is a good law. The Congress and the public should be proud of its existence and should reject any attempts to weaken or undermine it.

DMSO BACKGROUND

DMSO, which is receiving increased public attention as a potential therapeutic agent, is a byproduct of the paper pulp industry. It was recognized in the 1940's as an industrial solvent. It was not until it was discovered to penetrate skin rapidly that it attracted attention as a possible therapeutic agent; the first study of DMSO in humans under a "Notice of Claimed Investigational Exemption for a New Drug" (IND) was authorized in 1963, although some human use occurred even earlier.

Use of DMSO, especially for the treatment of sprains, bruises and minor burns, expanded quickly; by late 1965, an estimated 100,000 patients had been treated. No well-controlled studies were conducted, however, to prove that the alleged therapeutic effects were necessarily due to the drug. Furthermore, it was discovered that the drug changed the refractive index of the lens of the eyes in experimental animals. On November 25, 1965, by Federal Register publication, FDA terminated all clinical use of DMSO; concern at the time was that visual damage might occur in humans exposed to the drug.

This policy was revised a year later to allow renewed studies in serious conditions for which no satisfactory therapy was available, such as scleroderma, persistent herpes zoster, and severe rheumatoid arthritis. The Agency revised the statement of policy further in 1968 to permit

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topical application of DMSO for no more than 14 days for less serious disabilities such as acute musculo-skeletal conditions (e.g., sprains, bursitis, and tendinitis). This latter revision was based on a toxicological study in humans involving short-term topical application of DMSO, which showed no eye toxicity due to DMSO. Studies of long-term topical application also became available at about the same time. Since 1968, other regulations, notably the regulation that requires a 30-day FDA review period before a study under an IND may commence, have been published obviating the need for a specific regulation for clinical testing of DMSO. Thus, on September 21, 1979, the Agency published a Federal Register proposal to revoke the antiquated policy statement. The final order was published on May 13, 1980. Mr. Chairman, I would like to submit for the record copies of these publications.

NAS STUDY

In 1972, because of continuing controversy about DMSO, FDA asked the National Academy of Sciences to review all available information on the effectiveness and toxicity of DMSO and provide FDA with a report. The Academy report stated that there was inadequate evidence of effectiveness of DMSO for the treatment of any disease, that the toxicity potential was sufficiently great that the drug should remain an investigational drug, and that the controlled clinical investigations were necessary to demonstrate the effectiveness of DMSO. This independent report buttressed the Agency position on these issues. I would like to submit a copy of the Academy's report for the record.

NEW DRUG APPLICATIONS (NDAs)

During the 1960's three major drug firms considered the possibility of marketing DMSO commercially as a human drug under approved new drug applications, but all later lost interest. However, applications to treat swelling from trauma in horses and dogs were approved in the early 1970's.

Since the Academy's report, NDAs for DMSO have been submitted to FDA for two uses: scleroderma (an eventually fatal disease involving various internal organs and the skin, and which causes ulcers of the fingers and toes), and chronic interstitial cystitis (a painful bladder condition). A new drug application for use of 50 percent DMSO in the symptomatic relief of chronic interstitial cystitis was approved in 1978.

Research Industries Corporation, Salt Lake City, Utah, sponsor of the chronic interstitial cystitis application, also submitted in 1978 an NDA to market DMSO for scleroderma with claims limited to the symptomatic relief of pain and ulceration in the fingers. After detailed review by the Bureau of Drugs staff and by our Arthritis Advisory Committee, a group of nongovernmental experts, the application was found not approvable on the grounds that the clinical trials have not demonstrated that DMSO is effective for this use. At the request of several Members of Congress, we are performing another indepth review of this application.

Because of the possibility that DMSO may be useful in treating the hands of patients with scleroderma, we believe a properly controlled study should be conducted to demonstrate whether the drug is effective or not for this condition.

We, therefore, contacted representatives of the Cooperative Systemic Studies for Rheumatic Diseases Group (CSSRDG), which is supported by a contract from the National Institutes of Health. It is our understanding that the group currently is organizing a clinical study of DMSO in the treatment of scleroderma ulcers. This study is to be controlled in such a way as to obviate the problems of past studies.

Meanwhile, persons afflicted with scleroderma ulcers may seek to obtain the drug through their physicians under the investigational drug provisions of the law. Their physicians should contact Research Industries Corporation.

INVESTIGATIONAL APPLICATIONS (INDs)

Among the diseases which have been studied or are under study to determine the safety and effectiveness of DMSO are: interstitial cystitis, scleroderma, genital herpes, herpes zoster, amyloidosis, arthritic conditions of joints, tendinitis, bursitis, acute spinal cord injury, stroke, retinitis pigmentosa (a chronic progressive degenerative disease of the retina), and certain conditions of mental retardation. It is also being studied as a bone marrow cryopreservative. At the present time there are 24 active DMSO INDs on file, including sponsorship by some major firms.

There are no well-controlled DMSO studies being conducted under INDs for the treatment of rheumatoid arthritis or osteoarthritis and no NDA is before the Agency for approval of DMSO for these conditions. Yet the drug

is widely promoted for arthritis, and clinics or health centers have opened in several States where people are receiving treatments with DMSO administered topically, orally, and even by intravenous injection.

It is important to note that there is no regulatory barrier to the evaluation of DMSO for arthritis or any other condition. Our sole interest is in seeing that research on DMSO is well conducted scientifically so that meaningful data result and that studies are conducted safely under the usual ethical and scientific standards that apply to all human research.

Because there is a feeling among some physicians that DMSO may be useful in the treatment of soft tissue disorders such as sprains, strains, and other injuries, FDA invited Research Industries Corporation to meet with members of our Bureau of Drugs to discuss design and execution of clinical trials. The firm accepted and a meeting was held in April. Discussion also included the design of studies for radiation cystitis, a painful condition occurring after x-ray therapy for malignancy, and for other bladder conditions.

MISUSE OF DMSO

DMSO has been receiving extensive publicity in the news media with recent attention directly attributable to a Sixty Minutes segment which was shown on national TV in March and again in July. And because DMSO is widely available as an industrial solvent, as an approved veterinary drug product for the treatment of dogs and horses, as an

approved human drug for chronic interstitial cystitis, the drug is being used for a variety of conditions for which it has not been shown to be safe and effective.

In recent weeks, we in the FDA have become increasingly concerned about the growing use of DMSO in the health facilities I mentioned a moment ago, and also its widespread use for self-medication. People are being encouraged to purchase the industrial grade material and the veterinary product for self-treatment of various aches, sprains, arthritis, etc. Newspaper accounts from the State of Washington describe one situation where seven thousand pints of DMSO labeled as "industrial degreaser" have been sold by a general store. Similar accounts in other States have been reported.

FDA is concerned about the use of the drug in this manner and is attempting to assess the national scope of this practice, as well as to obtain information on the chemical quality and purity of the DMSO which is being offered through these sources.

Our concern over this widespread use is the risk that may accompany use of the industrial grade of DMSO, as well as the use of any DMSO in high concentrations and large amounts, and the potential that DMSO has, as a "carrier" chemical, to deliver harmful substances in the bloodstream if they are present in impure DMSO or on the skin. This concern caused us to issue a press release on July 25, 1980, to inform the public of these potential dangers. I would like to submit a copy for the record. Other information, which I will now briefly relate, also contributed to our belief that the public should be cautioned about the use of DMSO.

CURRENT ENFORCEMENT ACTIVITIES

Since we last testified before Congress on DMSO there have been unsettling revelations involving the clinical investigation of DMSO. As a result of routine inspections under our Bioresearch Monitoring Program.

Inspections have revealed, in the case of at least one clinical investigator, problems of such a serious nature that the clinical investigator is now ineligible to receive investigational drugs and conduct clinical studies. Specifically, our inspections showed that many of the required eye examinations reported as "normal" were never in fact performed and that adverse reactions to the drug may have occurred and were not reported to FDA. The seriousness of this incident is even more significant, as the study conducted by this investigator was relied upon by the Agency in the approval of the new drug application for chronic interstitial cystitis. We are continuing to investigate the matter in all aspects.

In another recent development, we received information that renewed our previous concern about the possibility of ocular toxicity. In March of this year, during a routine inspection of a clinical investigator conducting DMSO studies on scleroderma, FDA investigators found a 1977 letter in which the clinical investigator reported to the sponsor that some of his patients receiving DMSO had developed eye changes, possibly like those occurring in animals. Although our regulations require that the sponsor report all adverse reactions to FDA, our files reveal no report of these eye changes. This is the first instance where we have encountered a report of human eye toxicity in a DMSO study and we have initiated an extensive investigation of these findings, including review of the medical records by a consultant

ophthalmologist in addition to our own staff, to explore further whether the reported eye changes may be related to the use of DMSO and to determine whether violations of Federal laws have occurred.

In addition, we are requiring that eye examinations be conducted as part of any study involving chronic administration of DMSO in order to obtain additional data to determine whether the drug causes ocular toxicity. The labeling for the approved human drug product suggests that patients should receive thorough eye evaluations, including slit lamp examinations, prior to and periodically during treatment.

We are now in the process of auditing the data on studies of chronic interstitial cystitis conducted by other investigators to determine the quality and validity of those data and whether the practice of clinical investigation met the required standards of quality. Also, we have issued inspection assignments to audit the data of the scleroderma studies. In all of these investigations our staff is being asked to pay particular attention to whether or not these studies included eye examinations.

Finally, I must note that there has been some disagreement between the Bureau of Drugs staff and Bureau management concerning the inspectional approach to be taken by FDA investigators in conducting the several field investigations related to DMSO. This has resulted in an internal investigation by the Inspector General of the Department and another, at my direction, by the Associate Commissioner for Regulatory Affairs and the General Counsel. However, the Inspector General has requested that we suspend our internal investigation pending completion of theirs.

CONCLUSION

Although we continue to be dismayed on occasion by the findings uncovered through our Bioresearch Monitoring Program, it is gratifying to know that the program is doing what it was designed to do. Mr. Chairman, I am sure you feel a sense of satisfaction in knowing that your efforts to expand and fund this program had much to do with its success.

And, despite the current inspectional findings clouding the validity of the data reported to us on DMSO, we remain interested in the potential of the drug as a therapeutic agent and in controlled studies on its safety and effectiveness. At this time, other than for chronic interstitial cystitis (and that is currently under question), there are no adequate and well-controlled studies supporting the many other claims that have been made for DMSO.

Mr. Chairman, I would be pleased to answer any questions you or other Subcommittee Members may have.

E. L. EXHIBIT #15
NO. IND-19-718
DATE 3-29-78-TD
REPORTER MARSHALL

CLEVELAND CLINIC

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DEPARTMENT OF RHEUMATIC DISEASES
C. L. Hanson, M.D. C. B. Wilson, M.D.
A. M. Craig, M.D. T. L. Cleave, M.D.

May 4, 1977

Mr. Henry Moyle
RESEARCH INDUSTRIES, INC.
1847 West, 2300 South
Salt Lake City, UT 84119

Dear Mr. Moyle:

I am sending you clinical reports from nine of eleven patients with severe progressive systemic sclerosis who have been receiving dimethyl sulfoxide (DMSO) by oral administration. The two remaining patients will be returning for follow-up evaluation within the next month and I will forward their reports to you at that time.

These patients have been receiving a total daily dose of DMSO ranging from 21 gm to 84 gm in four divided doses diluted in concentrated juice and crushed ice. The duration of treatment has ranged from one month to 22 months with a mean average of 9.4 months.

You will note from the enclosed records that these patients had significant relief of pain related to the cutaneous ulcers, improved healing of chronic ulcers, and in some patients skin softening appeared which was associated with increased finger movements as well as increased strength in the hands.

In four of eleven patients reported at this time, nuclear sclerosis or progressive myopia have appeared during the study. One patient, Mr. LS age 67, showed early nuclear sclerosis before treatment was started. The lesions progressed slowly over a period of 22 months during which time our ophthalmologists have been of the opinion that there was nothing unusual about the clinical course of the nuclear lesions. However, two patients, Mrs. JB age 44 and Mrs. PF age 67, showed no evidence of nuclear sclerosis before treatment was started. Both of these patients now have nuclear sclerosis six months and eleven months, respectively, after the onset of treatment. Another patient, Mrs. KR age 50, shows a progressive myopic change which has appeared during her treatment the past six months. This patient, however, was complaining of mild blurring vision prior to the onset of treatment with DMSO and had previously been receiving large doses of corticosteroids. A refraction for new glasses was obtained before treatment with DMSO was started. A recent eye examination six months after DMSO was started shows an increase in myopia.

It is interesting to note that another patient in this group, Mr. CN age 57, had rapid appearance of cataracts just prior to the onset of progressive systemic sclerosis. He had cataract surgery with removal of both lenses prior to the onset of DMSO administration. Any relationship of progressive nuclear sclerosis to progressive systemic sclerosis has, not to my knowledge, been reported in the literature.

A review of the literature reveals only a few studies describing the eye lesions in patients with progressive systemic sclerosis. An article in the most recent "Annals of Rheumatic Disease" described ocular lesions in a group of patients with progressive systemic sclerosis, but no mention is made of nuclear sclerosis. This article also contains a sizable bibliography on ocular lesions in progressive systemic sclerosis but again no mention is made of these lesions.

In our previous study on the use of topical DMSO submitted to you, we did have a few patients with early nuclear sclerosis before treatment was started. It was noted that progression of these lesions was not apparent during the study.

In the first patient seen with progressive nuclear sclerosis (Mr. LS) our ophthalmologists did not suspect a relationship between DMSO treatment and the appearance of cataracts. However, the rapidity of the eye lesions in two patients, Mrs. JB and Mrs. PF, led our ophthalmologists to suspect that there may be a relationship between these lesions and oral DMSO therapy. Consequently, we have discontinued oral administration of DMSO in these four patients, despite their obvious need for treatment of the large complicating cutaneous ulcers over various areas of the body. One of these patients has extensive calcinosis cutis in addition to multiple deep ulcers which had been draining for four years and heretofore had responded to no type of therapy. The patient stated that this was the first time improvement in her condition had resulted from any form of treatment. Treatment was stopped and the patient was advised to return in two months for further evaluation. Mrs. JB had been allowed to continue topical DMSO because of her extensive ankle lesions which heretofore had not responded to any form of therapy. Oral DMSO was discontinued at this time. She will also return in two months for follow-up evaluation including an eye examination. Mrs. KR with early myopic changes has also been advised to discontinue oral DMSO and return in two months for follow-up evaluation.

I will keep you informed of any changes that occur in these patients. If you have any questions about clinical findings or our interpretations of these findings, please contact me.

Sincerely yours,

Arthur L. Scherbel, M.D.
Head, Department of Rheumatic Disease

ALS:cac

TO: Michael Hensley
HFD-180, Room 8-81
Parklawn

1 page

From: Jerry M. Baker
SIC-RP
588-5285

RESEARCH INDUSTRIES CORPORATION

May 9, 1977

Arthur Scherbel, M.D.
Cleveland Clinic
9500 Euclid Avenue
Cleveland, Ohio 44106

Dear Doctor Scherbel:

We received your most recent reports on the Scleroderma studies. We will be most anxious to see how these "Myopia" cases are progressing in your next report.

Thank you so much for all of your help.

Very truly yours,

RESEARCH INDUSTRIES CORPORATION
Pharmaceutical Division

Henry D. Moyle

HENRY D. MOYLE,
President

HDM/vh
signed by vh in HDM's absence

IND # 13,097

RESEARCH INDUSTRIES CORPORATION

May 16, 1977

Merle L. Gibson, M.D.
Director, Division of Anti-Infective Drug Products
Bureau of Drugs
Department of Health, Education and Welfare
FOOD AND DRUG ADMINISTRATION
Rockville, Maryland 20852

Dear Doctor Gibson:

Enclosed herewith, in triplicate, are copies of Arthur Scherbel, M.D.'s most recent progress reports on patients involved in the oral DMSO study on scleroderma under IND # 13,097.

Very truly yours,

RESEARCH INDUSTRIES CORPORATION
Pharmaceutical Division

HENRY D. HOYLE,
President

HDH/vb

Encl.

Salt Lake City Reg. Post

Mike Hensley
HFD-180

50

HFD-180
Room 86
Mike Hensley

RESEARCH INDUSTRIES CORPORATION

May 17, 1977

Arthur Schenkel, M.D.
Cleveland Clinic
9500 Euclid Ave.
Cleveland, Ohio 44106

Dear Doctor Schenkel:

During our most recent conference with Dr. Paul at the F.D.A. on May 16, 1977, Dr. Jacob and I showed him your letter of May 5, 1977, covering clinical reports from nine of your eleven patients with severe progressive systemic sclerosis, who have been receiving oral administrations of DMSO. Upon reading your letter, Dr. Paul suggested that we use the data accompanying your letter as supporting historical data for our IND # 13,092. Dr. Paul and Jacob suggested that we lower the dosage to less than 0.3 grams per Kilogram, with no DMSO intake two days a week.

Dr. Jacob will talking to you about dosage.

Best personal regards.

Yours very truly,

RESEARCH INDUSTRIES CORPORATION
Pharmaceutical Division

HENRY G. SMYTH
President

HGS/vh

IND # 10,778

RESEARCH INDUSTRIES CORPORATION

September 7, 1978

Merle L. Gibson, M.D.
Director, Division of Anti-Infective Drug Products
Bureau of Drugs
Department of Health, Education and Welfare
FOOD AND DRUG ADMINISTRATION
Rockville, Maryland 20857

Dear Doctor Gibson:

In response to the letter from your department dated August 7, 1978, the following is a summarized progress report on our IND # 10,778 employing the use of a 70% topical solution of DMSO for the treatment of patients with progressive systemic sclerosis.

Our investigations under this IND are still ongoing but to date our investigators have reported no abnormalities relating to the toxicity of the drug, nor have they reported any ocular abnormalities.

All updated patient reports throughout the year have previously been forwarded to the F.D.A. under separate cover.

Very truly yours,

RESEARCH INDUSTRIES CORPORATION
Pharmaceutical Division

HENRY D. MOYLE,
President

Office Copy

E. I. Exhibit #16
Mtr. IND 10-778
Date 3-26-82-20
Inspector MRHOR

CLEVELAND CLINIC

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DEPARTMENT OF RHEUMATIC DISEASE

A. L. Schertzer, M.D. — C. S. White, M.D.
A. H. Mackinnon, M.D. — N. J. Schnaper, M.D.
J. D. Cobum, M.D. — W. S. Wilson, M.D.
R. S. Brownell, M.D.

September 14, 1979

Henry D. Moyle, President
Research Industries Corporation
1847 West 2300 South
Salt Lake City, Utah 84119

Dear Mr. Moyle:

I am sending you case reports from six patients with progressive systemic sclerosis (generalized scleroderma) who have been treated with oral or parental Dimethyl Sulfoxide. All of these patients were seriously ill with rapidly progressive disease and the long-term prognosis was guarded or poor in each instance.

These patients have been treated for variable periods of time ranging from 18 months to 51 months, however, during these periods of time oral administration of DMSO was frequently discontinued for variable periods of time because of patients compliance or clinical improvement that occurred which is difficult to prove that the disease course has been altered because of the type of patient receiving treatment, the number of drugs used, the difficulty in randomization and the impossibility to prevent both the patient and the physician from knowing that DMSO was being administered. However, it is readily apparent at this time that all patients reported have noted significant symptomatic relief and they have benefited from the use of DMSO.

In most patients improvement occurred more rapidly initially during the first few months of treatment despite continuation of treatment. None of these patients were treated solely with DMSO, and most of them had received large doses of systemic corticosteroids, vasodilators and non-steroidal anti-inflammatory agents.

In those patients with refractory ulcers healing occurred more rapidly with parenteral administration of DMSO as compared with topical treatment. In all patients there was significant softening of the skin when DMSO was administered parenterally or orally as compared to the topical administration of the drug.

Cataracts were present in all patients in this group. One patient who never received corticosteroids had bilateral cataract extractions prior to coming to the Cleveland Clinic for DMSO treatment. I have reviewed the ophthalmological literature regarding the relationship of cataracts to systemic sclerosis. There are several reports describing the association of cataracts and systemic sclerosis.

The relationship between cataracts and the administration of systemic corticosteroids is well known. It is reported that there is no direct relationship between dose of corticosteroids, duration of treatment and the incidence of cataracts.

While toxicity has not been apparent these patients do have a strong breath odor that occurs with oral or parenteral administration. This unpleasant odor will certainly prevent wide spread use of the drug by these methods of administration of Dimethyl Sulfoxide.

I firmly believe that it will not be possible to carry out double blind studies in patients of this type with this method of drug administration. Perhaps an agreement can be made with the FDA to use this drug strictly for humanitarian purposes in those patients who are refractory to other methods of treatment.

Sincerely,

Arthur L. Scherbel, M.D.
ALS:rl

POSSIBLE ADVERSE EFFECTS NOT REPORTED DURING HPD-180 REVIEW
(Ophthalmic Patholo[illegible], Not Included)

Subject Identification	Study	Possible Adverse Effect	Reported? To Sponsor?	FDA?	Timely?
(1) MK	topical scleroderma	nausea, vomiting, diarrhea	Yes	No	
(2) CW	interstitial cystitis	chemical cystitis	Yes	No	
(3) MF	topical scleroderma	renal shutdown	Yes	No	
(4) MJ	interstitial cystitis	knots on arms and legs (phlebitis)	Yes	Yes	No
(5) JW	interstitial cystitis	chemical cystitis	Yes	Yes	No
(6) HBM	topical scleroderma	urticarial sheals at site of application	Yes	Yes	Yes
(7) JW	topical scleroderma	"get full occasionally and have to throw up"	Yes	Yes	Yes
(8) BS	interstitial cystitis	diminished white blood cell count	Yes	No	No
(9) DS	interstitial cystitis	bladder cancer	No	No	No
(10) IB	interstitial cystitis	chemical cystitis (bladder pain)	No	No	No
(11) ER	interstitial cystitis	chemical cystitis	Yes	Yes	No
(12) MM	interstitial cystitis	pain(s) (? chemical cystitis)	Yes	Yes	No
(13) EO	interstitial cystitis	chemical cystitis	Yes		
(14) CM	interstitial cystitis	bad taste in mouth	Yes	No	
(15) DS	interstitial cystitis	"hurting in bladder after each instillation"	Yes	No	
(16) EW	interstitial cystitis	"severe pelvic and penile pain", "cold sweat", and dysuria	Yes	No	

-Numerical base 55 patient audits

-Incidence of possible adverse effects 29%

Patient Name	DMSO Dose How Given	DMSO Dose Total Dose	Eye Problems During Study	Pertinent Medical History
AC	(a) topical (b) oral	unknown 0.36 gm/kg	-cataracts, senile type, noted after 10 years on topical - early cortical changes seen in right eye after 18 months on oral.	-51 years old. -took prednisone with DMSO
FW	(a) topical (b) oral	unknown 0.82 gm/kg	-pinpoint lesions in peripheral lenses after one year on topical DMSO - Very early nuclear sclerosis noted after 10 years on topical, one month on oral DMSO. -increased myopia and early nuclear sclerosis seen after 18 months on oral plus topical DMSO. These findings occurred at a time the patient was complaining of difficulty with distant vision. -subsequently complained of double vision at night.	-56 years old. -took prednisone with DMSO -prior to beginning oral DMSO was also treated with methotrexate.
LS	oral 4	0.41-0.55 gm/kg	-early cataract in left eye noted prior to study, rapidly progressed during the study, leading to surgical removal of lens after three years (received DMSO 2 years). -complained during study of sensation of a film over the left eye.	-67 years old. -took prednisone before and with DMSO.
PF	oral	0.53-0.71 gm/kg	-cortical opacities in the lenses and myopia, both noted after 4 months of oral DMSO. -these observations coincided with patient's complaints of blurred vision.	-66 years old. -took indomethacin with DMSO.
KR	(a) topical (b) oral	[redacted]	-first eye check not until one month after [redacted] started. Complained then of [redacted] difficulty."	-48 years old. -had been on prednisone for [redacted] years.

ORAL DMSO STUDY (continued)

Patient Name	DMSO Dose How Given	Total Dose	Eye Problems During Study	Pertinent Medical History
			-5 months after oral dosing starts findings were "minimal nuclear sclerosis" and "mild increase in myopic correction." -6 months after oral dosing starts patient says "last month I couldn't see far away, this month I can't see up close.	-had been getting DMSO from a veterinarian. -prednisone continued with DMSO.
TI	(a) clysis, with or without, (b) oral	combined doses to as much as 0.92 gm/kg per day.	-complains of blurred vision after 3 months on DMSO.	-20 years old. -prednisone before and during DMSO dosing.
JB	(a) topical (b) clysis, followed by (c) oral	unknown 0.77 gm/kg per day 0.64 gm/kg per day	-bilateral nuclear sclerosis with progressive myopia appeared during the study. Noted first after 11 months described as "rapidly progressive." -oral DMSO stopped 4/8/77 after discovery of eye lesions.	-43 years old. -treated previously with valisone a topical steroid. -history in chart describes "blurred vision" prior to the study.
HC	(a) topical	unknown	-very early nuclear sclerosis noted before study and did not worsen with DMSO. -complained of "eye strain" at near vision, off and on.	-58 years old. -no previous steroid treatment.
SH	(a) intravenous (b) oral (c) topical	0.45 gm/kg/day 0.25 gm/kg/day unknown	-nuclear sclerosis, mild, noted after 6 months.	-34 years old.

Subject Identification	Study	Ophthalmologic Finding	Reported to Research Industries?	Reported to FDA?	Timely?
(1) VM	Interstitial Cystitis	Cataracts, glaucoma prior to study and throughout (eye exams described as "normal" on CRFs)	No	No	
(2) GN	Interstitial Cystitis	"Clouding of lenses" noted several times	No (eye exams described as "normal" on CRF's)	No	
(3) MLM	Interstitial Cystitis	"Glaucoma, astigmatism history of retinal hole" prior to study	No (eye exams described as "normal" on CRFs)	No	
(4) MKD	Interstitial Cystitis	"Early senile changes in the crystalline lens," "senile macular degeneration," "senile cataract signs" after study	No (eye exams described as "normal" on CRFs)	No	
(5) GK	Scleroderma (topical)	"Early bilateral cateracts and peripheral irregular field defects," prior to study (7/10/75) "vision has changed from 20/60 -OD and 20/70 -OS, to 20/100 each eye. Her cataracts may have worsened and/or glasses need changing" (12/16/75) after 5 months on DMSO	Yes, at least in part. (Change in refraction may not have been	Yes	Yes
(6) SL	Interstitial Cystitis	Cataract or nuclear sclerosis prior to study ("posterior subcapsular dusting)	Yes	Yes (CRF says eye exams are "normal")	No

(7) LG	Interstitial Cystitis	Cataract or nuclear sclerosis prior to study ("nuclear sclerosis")	Yes	Yes No (CFR says eye exams are "normal")
(8) KK	Interstitial Cystitis	Cataract or nuclear sclerosis prior to study (nuclear sclerosis and peripheral cortical spicules)	Yes	Yes No (CFR says eye exams are "normal")
(9) RP	Interstitial Cystitis	Cataract or nuclear sclerosis during study ("faint cortical clouding")	Yes	Yes No (CFR says eye exams are "normal")
(10) MM	Interstitial Cystitis	Cataract or nuclear sclerosis during study (anterior and posterior subcapsular spokes)	Yes	Yes No (CFR says eye exams are "normal")
(11) AS	Interstitial Cystitis	Cataract or nuclear sclerosis during study ("early nuclear sclerosis, O.D.")	Yes	Yes No (CFR says eye exams are "normal")
(12) MW	Interstitial Cystitis	Cataract or nuclear sclerosis during study ("nuclear changes, OD" progressing to "early cataracts, bilateral")	Yes	Yes No (CFR says eye exams are "normal")
(13) RH	Interstitial Cystitis	Cataract or nuclear sclerosis prior to study ("nuclear sclerosis," apparently progressing to "cortical opacities")	Yes	Yes No (CFR notes NS prior to study implies no progression)

(14) AG	Topical and Oral Scleroderma	Cataracts during study	Yes	No
(15) PW	Topical and Oral Scleroderma	Peripheral lenticular opacities, nuclear sclerosis during study, increased myopia, visual difficulties	Yes	No
(16) LS	Oral Scleroderma	Cataract, prior to study, worsening during study ----- surgery	Yes	No
(17) PF	Oral Scleroderma	Cortical opacities in lenses, myopia, blurred vision during study	Yes	No
(18) KR	Topical and Oral Scleroderma	Minimal nuclear sclerosis, mild increase in myopia, visual difficulties during study	Yes	No
(19) TI	Parenteral, Oral Scleroderma	Blurred vision	Unknown	No
(20) JB	Topical, Parenteral, Oral Scleroderma	Bilateral nuclear sclerosis with progressive myopia appeared during the "study," "rapidly progressive"	Yes	No
(21) MC	Topical Oral	Very early nuclear sclerosis noted before study	Unknown	No
(22) SH	Parenteral, Oral, Topical Scleroderma	Nuclear sclerosis, mild, during study	Unknown	No

(23) MLA	Topical Scleroderma	"Few small white punctate cortical opacities, OD" during study	Unknown	No
(24) JO	Topical Scleroderma	"Few punctate cortical and posterior subcapsular changes in lens OS"during study	No	No
(25) CB	Topical Scleroderma	Complaints of double vision, "few fine punctate stains," both lenses, during study	Report to sponsor implies patient developed these prior to study - actually had been on DMSO several years before official study began and was normal prior to DMSO	No
(26) JM	Topical Scleroderma	"Early posterior subcapsular changes" bilateral, during study		
(27) MM	Topical Scleroderma	"Early nuclear changes" during study	No (CRF lists 10/74 eye exam we cannot find)	No
(28) IO	Topical Scleroderma	"Cortical cloudy" on right, "same plus dense spokes at periphery prior to study	Yes	Yes
(29) LGH	Interstitial Cystitis	"Refractive error" and "nuclear sclerosis" during study	No	No

(30) DS	Interstitial Cystitis	"Early cataracts" prior to study -- "Has noticed some skim over eyes" during study	Yes	No
(31) JW	Interstitial Cystitis	"Pterygium scars on cornea bilateral" some early lenticular opacities in OD, nuclear sclerosis," prior to study	No	No

CASE REPORTS HELD PRIOR TO NDA APPROVAL BY RIC

Subject identification	Therapeutic effect	Adverse effect	Did not obtain lab work	Did not perform eye exams	Other
CD	not listed				to be treated by local M.D. with DMSO
BP	poor				discontinued after 3 months because of poor therapeutic affect
HF	fair				to be treated by local M.D. with DMSO
LG	fair to good				to be treated by local M.D. with DMSO
JP	good				to be treated by local M.D. with DMSO
KP	fair				to be treated by local M.D. with DMSO
FM	not listed				to be treated by local M.D. with DMSO
MS	poor				
TS	fair				
MT	not listed				

Subject identification	Therapeutic effect	Adverse effect	Did not obtain lab work	Did not perform eye exams	Other
LT	not listed				to be treated by local M.D. with DMSO
JB	poor				no biopsy
EC	not listed				-diagnosis chronic active cystitis -to be treated by local M.D. with DMSO
RC	not listed				
EC	not listed				-no biopsy -probable single dose
LC	fair				-no biopsy -"symptoms of interstitial cystitis"
LG	fair to good				to be treated by local M.D. with DMSO
TW	good				diagnosis "chronic cystitis"
SR	excellent				began intravesicular DMSO in 1969

Subject identification	Therapeutic effect	Adverse effect	Did not obtain lab work	Did not perform eye exams	Other
CW	"none appreciable"	yes, chemical cystitis			
HA	good		yes	yes	CRF states patient being treated with DMSO by her doctor in Mexico City
HB	good		yes	yes	
LKN	good-excellent		yes	yes	
MH	good		yes	yes	no biopsy
WM	good		yes	yes	no biopsy
EO	fair and "did not show any appreciable response"	yes, chemical cystitis	yes	yes	
RP	good		yes	yes	
CV	good		yes	yes	
ER	good	yes, chemical cystitis			

CASE REPORTS HELD PRIOR TO NDA APPROVAL BY RIC

Subject identification	Therapeutic effect	Adverse effect	Did not obtain lab work	Did not perform eye exams	Other
KD					diagnosis "chronic cystitis"
NJ	fair	yes, "knots on arms and legs"			
EC	"absolutely no improvement"				diagnosis "prostatitis"
PS	not listed				diagnosis "chronic cystitis"
JG	fair		yes		no biopsy
JW	none			yes	
RB	excellent				diagnoses are "chronic prostatitis" and "cystitis cystica"
IB	excellent	yes, chemical cystitis	yes	yes	no biopsy
RS	not listed		yes	yes	no biopsy
DS	good	bladder cancer	yes	yes	no biopsy

Subject identification	Therapeutic effect	Adverse effect	Did not obtain lab work	Did not perform eye exams	Other
LS	fair		yes	yes	no biopsy
BS	not listed	yes, low white blood cell counts	yes	yes	no biopsy
BF	good		yes	yes	no biopsy
AM	good		yes	yes	no biopsy
MR	excellent		yes	yes	no biopsy
TC	not listed		yes	yes	no biopsy
GC	excellent		yes	yes	no biopsy
MM	good		yes	yes	no biopsy
CM	fair,"limited evidence of any significant benefit from DMSO"	yes, bad taste in mouth		yes	

Subject identification	Therapeutic effect	Adverse effect	Did not obtain lab work	Did not perform eye exams	Other
DS	fair, "no impressive affect of drug"	yes, burning in bladder with instillation, (chemical cystitis)	yes	yes	
RW	fair-good	yes, burning in bladder (severe) with cold sweat and painful urination		yes	interstitial cystitis with carcinoma of bladder
HC	worse				
FL	"no benefit from DMSO"		yes	yes	diagnosis prostatitis
AL	good		yes	yes	no biopsy
JW	not listed			yes	
RT	not listed		yes	yes	diagnosis urethritis and bladder neck contractures

Subject identification	Therapeutic effect	Adverse effect	Did not obtain lab work	Did not perform eye exams	Other
SB	not listed		yes	yes	no biopsy
ED	not listed, but "has helped her situation materially"		yes	yes	radiation cystitis
BC			yes		no biopsy

TOTAL 58

[Excerpt from the Federal Register, Vol. 44, No. 185
Friday, September 21, 1979--Proposed Rules]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[21 CFR Part 250]

[Docket No. 79N-0319]

Special Requirements for Specific Human Drugs, Revocation of Requirements for Dimethylsulfoxide

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to revoke the regulation that established specific requirements for the clinical testing and investigational use of dimethylsulfoxide (DMSO) in humans. The basis for the proposal is that the clinical testing and investigational use of DMSO can be adequately controlled under the agency's investigational new drug regulations and the special regulation concerning DMSO is no longer needed.

DATE: Written comments by November 20, 1979.

ADDRESS: Written comments to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Philip L. Paquin, Bureau of Drugs (HFD-30), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-5220.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of November 25, 1965 (30 FR 14639) FDA published a regulation (21 CFR 250.107) establishing specific requirements for the clinical testing and investigational use of DMSO in humans. This regulation was issued in response to findings linking the administration of DMSO to changes in the refractive index of the lens of the eyes of test animals. The regulation terminated all investigational new drug (IND) exemptions involving DMSO and established a preclearance requirement for investigations with the drug. The regulation has been amended twice: in the **Federal Register** of December 23, 1966 (31 FR 16403), to permit the investigation of certain unspecified "serious conditions," and in the **Federal Register** of September 10, 1968 (33 FR 12778), to further expand clinical investigations (in short-term studies for "benign conditions") and to drop the preclearance requirement.

The regulation served primarily as a way to publicize the agency's concern about the safety of human use of DMSO, to give notice that an IND was required before beginning clinical studies, to impose some specific limitations on the investigational use of DMSO, and to establish a preclearance requirement for investigations with the drug. It was particularly important to publicize the agency's concern about the safety of human use of DMSO because of the widespread availability of DMSO, a widely used industrial chemical, and the extensive publicity that it received as a miracle drug for several indications.

The regulation (21 CFR 250.107) imposes some specific limitations on the investigational use of DMSO, e.g., special requirements for long-term studies, and requires that certain examinations and diagnostic tests be performed on patients in the studies. For other investigational drugs, requirements such as these are imposed, where necessary, under the authority of Part 312 (21 CFR Part 312) and are modified as the studies progress on the basis of the information obtained from the studies. By contrast, the specific regulatory requirements for DMSO can be modified only by revising § 250.107, which procedure can unnecessarily delay modification of the study requirements. Thus, while this regulation does not give the agency any authority to regulate the investigation of DMSO not already provided by the IND regulations, it does have the disadvantage of making it necessary to use rulemaking procedures whenever the study requirements need to be changed.

The preclearance requirement was revoked in the September 10, 1968 amendment. The agency concluded at that time that the investigational use of DMSO could be adequately controlled by the imposition, by regulation, of the specific limitations on the investigational use of DMSO. Under those circumstances it was thought that preclearance was no longer necessary for the investigation of DMSO.

In the **Federal Register** of August 14, 1970 (35 FR 12891), the agency published a requirement that clinical studies for all drugs not be initiated until 30 days after the date the agency receives the IND (21 CFR 312.1(a)(2)). This requirement enables the agency to review IND submissions, including those for DMSO, before the studies are initiated, and thereby assure that the studies are to be conducted in accordance with all the appropriate restrictions. For these reasons, the agency has tentatively concluded that § 250.107 is unnecessary and should be revoked.

The agency's position on the investigational status of DMSO, and concern about the safety of human use of DMSO, is now widely known. If it is concluded that the information concerning DMSO needs further publicizing it will be done in the *Drug Bulletin* and by press release.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 701, 52 Stat. 1050-1053 as amended, 1055-1056 as amended (21 U.S.C. 352, 355, 371)) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1), it is proposed that Part 250 be amended by revoking § 250.107 *Dimethylsulfoxide (DMSO) preparations; clinical testing and investigational use.*

Interested persons may, on or before November 20, 1979, submit to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857, written comments regarding this proposal. Four copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the Hearing Clerk docket number found in brackets in the heading of this document. Received comments may be seen in the above office between 9 a.m. and 4 p.m., Monday through Friday.

In accordance with Executive Order 12044, the economic effects of this proposal have been carefully analyzed, and it has been determined that the proposed rulemaking does not involve major economic consequences as defined by that order. A copy of the regulatory analysis assessment supporting this determination is on file with the Hearing Clerk, Food and Drug Administration.

Dated: September 12, 1979.

Joseph P. Hile,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 79-29550 Filed 9-20-79; 8:45 am]

BILLING CODE 4110-03-M

[Excerpt from the Federal Register, Vol. 45, No. 94
Tuesday, May 13, 1980--Rules and Regulations]

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 250

[Docket No. 79N-0139]

Special Requirements for Specific Human Drugs Revocation of Requirements for Dimethylsulfoxide

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: This document revokes the regulation that established specific requirements for the clinical testing and investigational use of dimethylsulfoxide (DMSO) in humans. The Food and Drug Administration (FDA) is taking this action because clinical testing and investigational use of DMSO can be adequately controlled under the agency's investigational new drug regulations and the special regulation concerning DMSO is no longer needed.

EFFECTIVE DATE: June 12, 1980.

FOR FURTHER INFORMATION CONTACT: Philip L. Pequin, Bureau of Drugs (HFD-30), Food and Drug Administration, Department of Health and Human Services, 5600 Fishers Lane, Rockville, MD 20857, 301-443-5220.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of September 21, 1979 (44 FR 54730), the agency proposed to revoke § 250.107 (21 CFR 250.107). Section 250.107 served primarily as a way to publicize the agency's concern about the safety of the use of DMSO, to give notice that an investigational new drug (IND) exemption was required before beginning clinical studies, to impose some specific limitations on the investigational use of DMSO, and to establish a preclearance requirement for investigations with the drug. The agency had tentatively concluded that the regulation was unnecessary because FDA's position on the investigational status of DMSO is now widely known, and the investigational use of DMSO can be adequately controlled under the investigational drug regulation (21 CFR 312.1). No comments were received on the proposal.

§ 250.107 [Revoked]

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 701, 52 Stat. 1050-1053 as amended, 1055-1056 as amended (21 U.S.C. 352, 355, 371)) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1), Part 250 is amended by revoking § 250.107 *Dimethylsulfoxide (DMSO) preparations: clinical testing and investigational use.*

Effective date. This amendment is effective June 12, 1980.

(Secs. 502, 505, 701, 52 Stat. 1050-1053 as amended, 1055-1056 as amended (21 U.S.C. 352, 355, 371))

Dated: May 5, 1980.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 80-14477 Filed 5-12-80; 8:45 am]

BILLING CODE 4110-03-M

[Excerpt from the Federal Register, Vol. 30, No. 228
Thursday, November 25, 1965--Rules and Regulations]

Title 21—FOOD AND DRUGS

Chapter I—Food and Drug Administration, Department of Health, Education, and Welfare

SUBCHAPTER A—GENERAL

PART 3—STATEMENTS OF GENERAL POLICY OR INTERPRETATION

Dimethylsulfoxide (DMSO) Preparations; Termination of Clinical Testing and Investigational Use

Under the authority vested in the Secretary of Health, Education, and Welfare by the Federal Food, Drug, and Cosmetic Act (sec. 701, 52 Stat. 1055; 21 U.S.C. 371) and delegated to the Commissioner of Food and Drugs by the Secretary (21 CFR 2.90), the following statement of policy is issued:

§ 3.52 Dimethylsulfoxide (DMSO) preparations; termination of clinical testing and investigational use.

(a) Chronic-toxicity studies with dimethylsulfoxide (DMSO) in animals, including dogs, rabbits, and swine, reported by a consulting laboratory in England and by at least two laboratories in the United States show that the administration of dimethylsulfoxide (DMSO) causes changes in the refractive index of the lens in the eyes of such animals. On the basis of these reports, sponsors of investigations with dimethylsulfoxide (DMSO) have discontinued clinical testing of dimethylsulfoxide (DMSO) preparations in man. All exemptions for clinical testing of dimethylsulfoxide (DMSO) in man are hereby terminated effective on signature of this order. No person may ship dimethylsulfoxide (DMSO) within the jurisdiction of the Federal Food, Drug, and Cosmetic Act for clinical testing in man until his proposal for such studies has had advance approval by the Commissioner of Food and Drugs on the basis of a Notice of Claimed Investigational Exemption for a New Drug (form FD 1571) justifying such studies.

(b) On the basis of these reports, the Commissioner of Food and Drugs further finds that it is not safe to initiate or continue investigations with any preparation containing dimethylsulfoxide (DMSO) in animals other than animals used solely for laboratory research. The Commissioner of Food and Drugs hereby terminates, effective upon signature of this order, all exemptions under § 130.3 of this chapter and section 505 of the act, for the use of dimethylsulfoxide (DMSO) or any preparation containing any amount of dimethylsulfoxide (DMSO) for investigational use in animals, except in compliance with the provisions of § 130.3(f) of this chapter, in animals used solely for laboratory research purposes and which are not to be used subsequently for food production.

(c) Sponsors of all clinical investigations with dimethylsulfoxide (DMSO) should immediately recall all outstanding stocks of investigational drugs containing dimethylsulfoxide (DMSO) except those involving investigations in laboratory animals.

(Secs. 505, 701(a), 52 Stat. 1052 as amended 52 Stat. 1055; 21 U.S.C. 355, 371(a).)

Dated: November 19, 1965.

GEO. P. LARRICK,
Commissioner of Food and Drugs.

[F.R. Doc. 65-12877; Filed, Nov. 24, 1965; 8:45 a.m.]

[Excerpt from the Federal Register, Vol. 31, No. 248
Friday, December 23, 1966--Rules and Regulations]

Title 21—FOOD AND DRUGS

Chapter I—Food and Drug Administration, Department of Health, Education, and Welfare

SUBCHAPTER A—GENERAL

PART 3—STATEMENTS OF GENERAL POLICY OR INTERPRETATION

Dimethylsulfoxide (DMSO) Preparations; Clinical Testing and Investigational Use

In the FEDERAL REGISTER of November 25, 1965 (30 F.R. 14639), a statement of policy (21 CFR 3.52) was published concerning the termination of clinical testing and investigational use of dimethylsulfoxide (DMSO) preparations. A recent comprehensive evaluation of all available data on dimethylsulfoxide (DMSO) indicates that the drug may be of value in treating certain serious conditions which justify further clinical investigations. Accordingly, under the authority vested in the Secretary of Health, Education, and Welfare by the Federal Food, Drug, and Cosmetic Act (secs. 505, 701(a), 52 Stat. 1052, as amended, 1055; 21 U.S.C. 355, 371(a)) and delegated by him to the Commissioner of Food and Drugs (31 CFR 2.120; 31 F.R. 3008), § 3.52 is revised to read as follows:

§ 3.52 Dimethylsulfoxide (DMSO) preparations; clinical testing and investigational use.

(a) Chronic-toxicity studies with dimethylsulfoxide (DMSO) in animals, including dogs, rabbits, and swine, reported by a consulting laboratory in England and by a number of laboratories in the United States show that the administration of dimethylsulfoxide (DMSO) causes changes in the refractive index of the lens in the eyes of such animals. On the basis of these reports, clinical testing of dimethylsulfoxide (DMSO) preparations was discontinued for a time and later resumed under very restricted conditions.

(b) A recent comprehensive evaluation of all available data on dimethylsulfoxide (DMSO) preparations indicates that the drug may be of value in treating certain serious conditions which justify further clinical investigation.

(c) No person may ship dimethylsulfoxide (DMSO) within the jurisdiction of the Federal Food, Drug, and Cosmetic Act for clinical testing in man until the proposal for such studies has had advance approval by the Commissioner of Food and Drugs on the basis of a Notice of Claimed Investigational Exemption for a New Drug (Form FD 1571, described in § 130.3(a)(2) of this chapter) justifying such studies.

(d) The Commissioner may approve proposed clinical studies involving the administration of dimethylsulfoxide (DMSO) preparations to man provided that all of the following conditions are met:

(1) The proposed study restricts the use of dimethylsulfoxide (DMSO) to cutaneous application in serious conditions, such as scleroderma, persistent herpes zoster, and severe rheumatoid arthritis, for which no satisfactory therapy is now available.

(2) The proposed study will be conducted in a medical center having adequate facilities and well-trained, experienced medical personnel.

(3) The proposed study provides that all subjects will receive a full examination:

(i) Including eye evaluation by ophthalmologists prior to receiving the drug, at intervals not exceeding 3 months during the study, and 3 months after discontinuing the drug; and

(ii) Including liver function tests and blood tests, prior to receiving the drug, at intervals not exceeding 4 weeks during the study, and 4 weeks after discontinuing the drug.

(4) The proposal shows that patient consent requirements will be carefully observed and includes a commitment that patients will be fully informed of the effects of dimethylsulfoxide (DMSO) in animals and of the possibility that these may occur in humans.

(e) Dimethylsulfoxide (DMSO) preparations may be shipped within the jurisdiction of the act solely for tests in vitro and in laboratory research animals in accord with the provisions of § 130.3a(a) of this chapter.

(f) No person may ship dimethylsulfoxide (DMSO) within the jurisdiction of the act for clinical investigation in animals as provided in § 130.3a(b) of this chapter until his proposal for such studies has had advance approval by the Food and Drug Administration on the basis of the submission of information in accord with the provisions of § 130.3a(b) of this chapter.

(secs. 505, 701(a), 52 Stat. 1052, as amended, 1055; 21 U.S.C. 355, 371(a))

Dated: December 19, 1966.

JAMES L. GODDARD,
Commissioner of Food and Drugs.

[F.R. Doc. 66-13789; Filed, Dec. 22, 1966; 8:49 a.m.]

[Excerpt from the Federal Register, Vol. 33, No. 176
Tuesday, September 10, 1968--Rules and Regulations]

Title 21—FOOD AND DRUGS

Chapter I—Food and Drug Administration, Department of Health, Education, and Welfare

SUBCHAPTER A—GENERAL

PART 3—STATEMENTS OF GENERAL POLICY OR INTERPRETATION

Dimethylsulfoxide (DMSO) Preparations; Clinical Testing and Investigational Use

A statement of policy, § 3.52, concerning clinical testing and investigational use of dimethylsulfoxide (DMSO) preparations was published in the FEDERAL REGISTER of November 25, 1965 (30 F.R. 14819), and revised December 23, 1966 (31 F.R. 16463). A previous evaluation of all data available on DMSO indicated that further clinical investigations in treating certain serious clinical conditions were justified.

Data are now available establishing that short-term use of DMSO involving application of not more than 1 gram of DMSO per kilogram of body weight for not more than 14 consecutive days will be reasonably safe. Therefore, in addition to long-term clinical studies in serious conditions, short-term clinical investigation of DMSO for relatively benign conditions can be justified. Also, additional information is required to evaluate the possible relationship and the incidence of certain subtle toxic manifestations of DMSO on the liver and the hemopoietic system. The next step in the investigation is adequately monitored short-term trials on a limited number of patients (Phase II), involving cutaneous application of DMSO, in order to obtain the essential information described above prior to consideration of the initiation of broader clinical studies (Phase III).

Accordingly, under the authority vested in the Secretary of Health, Education, and Welfare by the Federal Food, Drug, and Cosmetic Act (secs. 505, 701(a), 52 Stat. 1052-53, as amended, 1055; 21 U.S.C. 355, 371(a)) and delegated to the Commissioner of Food and Drugs (21 CFR 2.120), § 3.52 is revised to read as follows:

(Note: This revision revokes the requirements of preclearance of dimethylsulfoxide (DMSO) for clinical testing in man and in animals.)

§ 3.52 Dimethylsulfoxide (DMSO) preparations; clinical testing and investigational use.

(a) (1) Chronic-toxicity studies with dimethylsulfoxide (DMSO) in animals, including dogs, rabbits, and swine, reported by a consulting laboratory in England and by a number of laboratories in the United States show that the administration of dimethylsulfoxide (DMSO) causes changes in the refractive index of the lens of the eyes of such animals. On the basis of these reports, clinical testing of dimethylsulfoxide (DMSO) preparations was discontinued for a time and later resumed under restricted conditions.

(2) An adequate, controlled human toxicity study (Phase I) involving short-term cutaneous application of 1 gram of dimethylsulfoxide (DMSO) per kilogram of body weight daily for 14 consecutive days has recently been completed. Data obtained, not previously available, show that when dimethylsulfoxide (DMSO) was applied topically to the skin of healthy volunteers, it did not produce adverse effects upon the eyes of the subjects. Mild, apparently reversible, changes were seen suggesting that the drug may have some effect upon the liver and upon the hemopoietic system in some subjects.

(b) A comprehensive evaluation of all available data on dimethylsulfoxide (DMSO) preparations justifies further clinical investigation of the drug in treating certain serious conditions. Although reports concerning the use of dimethylsulfoxide (DMSO) in relatively benign conditions are equivocal regarding its efficacy, short-term clinical use has been established as reasonably safe by adequate Phase I studies. Under appropriate protocols, further short-term clinical investigations in the treatment of such benign conditions can be justified.

(c) No person may ship dimethylsulfoxide (DMSO) within the jurisdiction of the Federal Food, Drug, and Cosmetic Act for clinical testing in man until a "Notice of Claimed Investigational Exemption for a New Drug," pursuant to § 130.3 of this chapter, is on file with the Food and Drug Administration and all the following conditions are met:

(1) Proposed long-term clinical studies (Phase II) are restricted to the use of DMSO to cutaneous application in serious conditions, such as the incapacitating arthropathies, scleroderma, dermatomyositis, and intractible pain due to malignancy, are to be conducted in medical centers having adequate facilities and well-trained, experienced medical personnel, and are to include the following essential conditions in the study protocol. All subjects will receive a full examination including:

(i) An eye evaluation by an ophthalmologist to include actual refractive error measurements and slit-lamp findings as well as other parameters of the ocular examination prior to receiving the drug, at intervals not exceeding 3 months during the study and 3 months after discontinuing the drug.

(ii) Liver function tests and a complete blood count (CBC) prior to receiving the drug, at intervals not exceeding 4 weeks during the study and 4 weeks after discontinuing the drug.

(2) Proposed short-term studies (Phase II) restrict the use of dimethylsulfoxide (DMSO) to cutaneous application for not more than 14 days in closely monitored investigations, with appropriate control groups, that may include studies of use in such conditions as acute musculoskeletal conditions (acute arthritis, peri arthritis, capsulitis, bursitis, tendonitis, synovitis, and post-traumatic lesions) and soft tissue injuries. The proposed studies shall provide for pretreatment liver function studies and a complete blood count (CBC), to be repeated within 7 days after commencing treatment and at the conclusion of the study. Routine monitoring of effects upon the eye is not required.

(3) All proposals must show that patient consent requirements will be carefully observed and shall include a commitment that patients will be fully informed of: The effects of dimethylsulfoxide (DMSO) in animals, the possibility that these may occur in humans, and the known possible effects of the drug in humans.

(d) Dimethylsulfoxide (DMSO) preparations may be shipped within the jurisdiction of the act for tests in vitro and in laboratory research animals in accordance with § 130.3a(a) of this chapter and for clinical investigation in animals in accord with § 130.3a(b) of this chapter.

(Secs. 505, 701(a), 52 Stat. 1052-53, as amended 1055; 21 U.S.C. 355, 371(a))

Dated: August 30, 1968.

HERBERT L. LEY, JR.,
Commissioner of Food and Drugs.

[F.R. Doc. 68-10800; Filed, Sept. 9, 1968; 8:45 a.m.]

Senator KENNEDY. We will have Dr. Stanley Jacob, associate professor of surgery at the University of Oregon Medical School, and Henry Moyle, president of Research Industries, Salt Lake City.

Will the witnesses rise with me, please?

Do you swear that the testimony you give is the truth, the whole truth, and nothing but the truth, so help you God?

Dr. JACOB. I do.

Mr. MOYLE. I do.

Senator KENNEDY. Let the record show that both Dr. Jacob and Mr. Moyle responded affirmatively.

Mr. Moyle, maybe we will start the questioning with you, if we may, please. As I understand it, you are the president of Research Industries Corp., is that correct?

STATEMENT OF HENRY MOYLE, PRESIDENT, RESEARCH INDUSTRIES CORP., SALT LAKE CITY, UTAH, ACCOMPANIED BY LOUIS HAYNIE, RESEARCH INDUSTRIES CORP., SALT LAKE CITY, UTAH; AND STANLEY W. JACOB, M.D., ASSOCIATE PROFESSOR, DEPARTMENT OF SURGERY, UNIVERSITY OF OREGON MEDICAL SCHOOL, A PANEL

Mr. MOYLE. That is correct, Senator.

Senator KENNEDY. Would you tell us what business that organization was in originally and how you got into the DMSO business?

Mr. MOYLE. We incorporated Research Industries Corp. in 1968. It was an amalgamation of land and operations that was already in existence, and a drug operation that was already in existence known as Deseret Drug Co., which had all the pharmaceutical products of Deseret Pharmaceuticals, which is a Salt Lake City-based company.

Senator KENNEDY. And that is how you got into the DMSO business itself?

Mr. MOYLE. No; that is how we got into the drug business. We had a line of about 30 drugs that we got ultimately from Deseret Pharmaceutical. These drugs were pretty much me-two items. We learned a lot about drugs and a lot about marketing in the 4 or 5 years that we utilized those drugs.

In the early 1970's, my partner and I, Lou Haynie, who is here, discovered through a friend in San Diego that there were people being treated with a drug known as DMSO in Mexico, in a little town called Tecate. At Tecate, they were taking patients in for 3 days, giving them two treatments a day of 99-percent DMSO concentration all over their bodies.

Lou and I went down there and we viewed what was happening, and saw the results and talked to the people before and after, and found that there was an amazing result when they were treated with this drug. Most of those people had ailments that were arthritic in nature.

Eventually, we decided to buy three clinics in Mexico; one in Tecate, one in Nogales, and one in Juarez. We were treating patients in those three clinics under the direction of Mexican doctors. I was not quite satisfied that it was safe, so I discovered in some literature that I read the name Stanley Jacob.

I called him at his place at the University of Oregon; we arranged a meeting with him and a Dr. Don Wood, who was his

associate at that time. As a result of that meeting, Dr. Jacob and I toured the clinics in Mexico. I asked him the question, "Are we doing it OK; is there anything wrong with what we are doing; is there any potential harm that could befall these people that are being treated?"

When we were finished, Dr. Jacob came up with the conclusion that what we were doing was all right. He made a few suggestions which we followed, and we worked with those clinics for a period of time and then decided that trying to get Americans to come to Mexico was a back-door approach to working with the drug. We decided on a frontal attack, as it were, in the United States. We decided that we could work with the FDA in trying to get approval of this drug, because the results of use of the drug were dramatic.

At that time, we had the opportunity to contact the FDA. I was at that time introduced to Dr. K. C. Pani, and Dr. Pani, Dr. Jacob and myself discussed possibilities for approval of DMSO for various indications.

The two indications at that time that we came down to were two fairly intractable, untreatable diseases known as scleroderma and interstitial cystitis. There had been, I found out at that time, some doctors in the United States who had used DMSO in scleroderma and in interstitial cystitis; primarily, Dr. Scherbel in scleroderma and Dr. Stewart in interstitial cystitis at the Cleveland Clinic.

I checked the Cleveland Clinic and found that this clinic in the United States was one of the most respected clinics in the country. I checked Dr. Stewart and Dr. Scherbel and found that they were very well respected in their professions, and we could not think of anyone else who had the experience or the knowledge whom we could get to study these indications.

So, ultimately, in 1974 we initiated two IND's with the FDA; one on scleroderma and one on interstitial cystitis.

Senator KENNEDY. Now, is it fair to say that the drug manufacturing business was fairly new to you and to Research Industries Corp.?

Mr. MOYLE. Drug manufacturing, yes. With the drugs we had, we were primarily a distributor; someone else manufactured for us.

Senator KENNEDY. So your firm was generally inexperienced in dealing with the Food and Drug Administration prior to the submission of the NDA for DMSO?

Mr. MOYLE. Yes. That was our first shot at it; that is right.

Senator KENNEDY. What kind of in-house medical and scientific capability does Research Industries have?

Mr. MOYLE. Well, at the present time, we have a wholly owned subsidiary known as Tera Pharmaceuticals, located in Buena Park, Calif. We have a crew down there of about 20—well, it varies from 20 to 30 people. They are in the manufacturing business, and have been for a number of years. They used to be owned by Nutri-Lite, which was a wholly owned subsidiary, I believe, of Amway.

Senator KENNEDY. Do you have any breakdown of how many physicians you have, or how many scientists you have?

Mr. MOYLE. Well, our manager is Dr. Chapman Dunn. We have two chemists and others with chemistry background. Our salaried staff is five people.

Senator KENNEDY. Well, are there any physicians; do you have any physicians?

Mr. MOYLE. No; our head down there is a veterinarian, not a physician. Now, we do have physician monitors. To begin with, Dr. Jacob was our medical consultant and adviser and monitor. At this time, we have three doctor-physician monitors working with us on three different indications for the drug.

Senator KENNEDY. Who was the monitor for the DMSO studies when they were originally being done?

Mr. MOYLE. For scleroderma and interstitial cystitis, Dr. Jacob was the monitor for those two studies.

Senator KENNEDY. And what other relationship did Dr. Jacob have with Research Industries?

Mr. MOYLE. Dr. Jacob at one time was a director of Research Industries. He is no longer a director. Of late, he has been a consultant, consulting with us on various aspects of DMSO.

Senator KENNEDY. Is Dr. Jacob still the scientific monitor for DMSO?

Mr. MOYLE. No; he is not monitoring any indications at this time.

Senator KENNEDY. Why not?

Mr. MOYLE. We received a letter from the FDA advising us that at a prior meeting we had had with them, wherein Dr. Jacob stated that he really hardly had time to be monitor anymore because of his responsibilities at the University of Oregon—the letter from the FDA says, "Because of these responsibilities of Dr. Jacob, we would appreciate it if you would terminate his monitor relationship."

Senator KENNEDY. Does he have a financial interest in the company?

Mr. MOYLE. Well, I think he is better qualified to say that than I am. My understanding is that he now has 50,000 shares of stock in the company.

Is that correct?

Dr. JACOB. That is correct.

Senator KENNEDY. Dr. Jacob, is that substantially correct?

Dr. JACOB. That is correct, Senator Kennedy.

Senator KENNEDY. Just in terms of the size or the quantity, what is the value?

Mr. MOYLE. Research Industries has 2,050,000-some-odd shares outstanding.

Senator KENNEDY. What is the value of each share?

Mr. MOYLE. The market value today should be in the $12 area. It is a publicly traded corporation on NASDAC.

Senator KENNEDY. Do you have a contract to buy additional shares?

Dr. JACOB. Yes, I do. But we reached an agreement, in principle, in June relating to my severing my relationship with Research Industries.

Mr. MOYLE. That would also sever that if we finally worked that out formally; it has not been done formally yet.

Dr. JACOB. That is right.

Senator KENNEDY. What was the nature of the contract?

Dr. JACOB. Well, I received $2,000 a month as a medical consultant, and the contract allowed me to purchase additional shares of Research Industries stock over the next 4 years.

Senator KENNEDY. How much stock?

Dr. JACOB. Another 100,000 shares, Senator Kennedy.

Senator KENNEDY. Over the period of the next 4 years?

Dr. JACOB. Over the period of the next 4 years.

Senator KENNEDY. Did they set the price?

Dr. JACOB. Well, yes; 50,000 shares at $6.50, and 50,000 shares at $9.50.

Senator KENNEDY. Over the next 4 years?

Dr. JACOB. Yes, sir.

Senator KENNEDY. And you have 50,000 now, is that correct?

Dr. JACOB. Yes. I borrowed the money in July 1978, after approval, and I still owe on that. My plan at that point was, and still is—it was lettered stock—that when the stock is viable in terms of sale, which it now is, I planned to pay off the debts associated with purchase and contribute as much as I could to DMSO research.

I had the opportunity, Senator Kennedy, to buy stock early in the game at a very low price, but I turned it down because I did not want to be accused of any profit motive. In addition to that, when I helped make the discoveries relating to DMSO, I turned over all rights to the University of Oregon Health Sciences Center; at that time, it was the medical school. I have given all the royalties to the medical school for the Department of Surgery and for DMSO research. I plan to continue doing that.

Senator KENNEDY. How much were the shares in the very beginning when you bought them?

Mr. MOYLE. Our initial issue was $2 a share.

Senator KENNEDY. $2 a share?

Mr. MOYLE. Yes.

Senator KENNEDY. What did you pay for the initial shares, Dr. Jacob?

Dr. JACOB. $6.50 a share, Senator Kennedy.

Senator KENNEDY. All right.

Mr. Moyle, you heard the FDA testimony this morning about the inadequacy of the work done for you by Dr. Shirley. As I understand it, the NDA which is approved for DMSO is based on the two studies, one by Shirley and one by Stewart. The one by Shirley is now discounted as inadequate by the FDA, and questions were raised about the Stewart study.

With regard to the Shirley study, the FDA found a failure to maintain adequate and accurate case histories, a failure to maintain adequate records of drug accountability, a failure to obtain institutional review committee approval, and a failure to maintain documentation of adequate and informed consent.

As a part of this, FDA found that most of the required eye and laboratory examinations were, in fact, never performed at all. In addition, FDA found that in some of the cases report forms were, in fact, altered between the first FDA inspection and the second FDA inspection.

Now, whose responsibility would it be at Research Industries to detect these kinds of problems which apparently went undetected right through the NDA approval process?

Mr. MOYLE. Senator, I believe that the ultimate responsibility, certainly, lies with me. I signed the documents that went into the FDA. We had many people working with me. I certainly cannot shirk the responsibility. I did not know everything that was going on, but what I could find out, I found out. I found that when all this happened and Dr. Shirley called and said, "They have come to investigate the records," I told him to go ahead and show them everything he had.

Since that time, he has been back to each patient, and I understand he has had every patient in his office. He has obtained an affidavit from every single one of them, and every one of them says that they had some eye tests.

Now, Dr. Pani testified here today that the eye tests should have been prior to, during, and after the study. I am not positive that in every case they were done just that way, but there were eye exams before and after. There may have been one or two cases where there were not; I am not sure, but I believe that in a very substantial number of cases, according to the affidavits of those patients which we have sent to everyone, there were eye exams. I think that out of the 40 or 41 patients, there were 22 affidavits that had eye doctor letters attached stating they did the eye exams.

Now, the eye exams that were done were eye exams that were similar to those done on the animals—the slit lamp examination. We discussed this toxicity data with the FDA and it was determined that that was the way we should do it.

Senator KENNEDY. We are not scientists here. Let me find out, if I could, if Dr. Hensley is still in the room, why, the affidavits from the various doctors, that was not satisfactory. Mr. Moyle has indicated that the majority of them had eye tests and there were affidavits by doctors. Why did you find it inadequate?

Dr. HENSLEY. The only patients I can comment on are the 15 whom we chose for the audit; as I said, that was a random selection. We have visited those patients and I have compared their affidavits given to our investigators and our interviews of the ophthalmologists to the affidavits submitted by Research Industries, ostensibly obtained either from Dr. Shirley or from the patients this year. The two are quite different.

First of all, the Research Industries affidavits appear to be rather vague and general; they do not deal with the issues; "did you have the eye exam before, during, and after the study," as required by the Federal Register and by the protocol.

Second, I am afraid that we are going to have some problems from a regulatory point of view with the way those affidavits were drawn up.

Mr. MOYLE. Senator, I have no information as to whether they are accurate. I did not help in the preparation of those affidavits; Dr. Shirley mailed them to me and told me that they were—my belief is that they are substantially accurate records of those patients who each signed the affidavits separately.

Dr. JACOB. Senator Kennedy, you know, listening to the FDA testimony, I was appalled, because I really think that deliberately or not deliberately, there were major distortions.

Senator KENNEDY. All right. Well, we just want to follow through here, if we could, with Mr. Moyle and then we will give you a chance to give a response.

What would be the impact on Research Industries if, as a result of these problems, the FDA determined that it could no longer maintain the approval of DMSO for treatment?

Mr. MOYLE. Well, Senator, we are a small company. We believed when we started with this application that it would not take nearly this long, and we have stretched it out. On our marketing, we are not yet breaking even. So, we would have real problems. I suppose we would have to dispose of our subsidiary, Terra; that would be too expensive an operation to be able to continue with. If we did that, we would no longer have a lab approved for good manufacturing practices, and it took us 3 or 4 years to get that approval at the FDA. So, that would be an impossible burden; I do not know what we would do.

Senator KENNEDY. Now, is it fair to say that from the very beginning, one of the major concerns people have had about DMSO is the fact that it seems to have caused eye damage in animals, and therefore one had to be very careful to look at the comparable eye damage in humans?

Mr. MOYLE. Well, yes. My understanding, Senator, was that early in the game, there were some animal studies done; that the FDA at that time banned the use of the drug in the United States. Then, apparently, later on they again agreed to let it be used experimentally for clinical evaluations.

Senator KENNEDY. Well, now, the most serious allegation made thus far is that on May 4, 1977, Dr. Scherbel wrote to you describing some potential eye problems with patients who had used DMSO. The significance of these problems is not clear and they are certainly subject to further study.

The fact is that they were the first report of the potential human eye problems of patients on DMSO. The Scherbel letter requested very careful review by FDA. Yet, this material never found its way into the FDA file until 3 years after you had been alerted to it.

You heard the medical officer for the Food and Drug Administration, Dr. Pani, say that he was never aware of these findings; and that if he had been, he would have acted vigorously because of the critical nature of the findings. You were made aware of these findings on May 4, 1977, in a letter. You acknowledged these findings in your return letter to Dr. Scherbel, in which you said you would be most anxious "to see how these myopia cases were progressing in your next report."

Now, what did you do with the Scherbel letter, and did you believe it to be significant?

Mr. MOYLE. I feel that Dr. Pani is a real gentleman and a fine man and a great humanitarian, and we enjoyed our relationship with him. However, I must state here, Senator, that in company with Dr. Jacob, we had a meeting with the—I think we received that May 4 letter on about the 8th or 9th of May. On the 16th, we had a conference at the FDA on chemistry with Mr. John Richmond at the FDA. Also, that day I had a meeting with Dr. Garfis at the FDA.

That was the day when we presented the letter to Dr. Pani. Now, as to the content of the letter, all the eye doctors at the Cleveland Clinic and Dr. Scherbel all agreed that there was no DMSO-related toxicity.

Now, the FDA this morning has talked about a progressive toxicity of the eye in those patients. There may have been, but there is no evidence that it was DMSO-related, and I think that is the difference.

Senator KENNEDY. Well, we certainly are not going to be able to make that determination.

Mr. MOYLE. I asked Dr. Scherbel to come today and he said that he had not been invited, so that he is not here. He should be present.

Senator KENNEDY. The point is, it seems to me, is whether the information was provided to the agency.

Mr. MOYLE. As I say, we did provide it to Dr. Pani.

Senator KENNEDY. Well, Dr. Pani said you did not.

Mr. MOYLE. I heard his testimony and, as I say, I feel he is a gentleman and a fine man.

Senator KENNEDY. Well, there is a direct conflict here on a matter that the Commissioner says is of enormous importance and consequence.

Mr. MOYLE. Senator, allow me to elucidate, perhaps, a little more.

Senator KENNEDY. You say you did and he said he did not. Now, we cannot resolve that. All we can do is refer that to the Justice Department and let them make the judgment.

Mr. MOYLE. Well, that is fine.

Senator KENNEDY. I do not want to get into——

Mr. MOYLE. But I have one thing that reflects on this, if I may.

Senator KENNEDY. Yes.

Mr. MOYLE. At that meeting, it was decided that the dosage for oral DMSO should be reduced, and a change made in the protocol. That change was made and we wrote a letter pursuant to that meeting to make the change. That is the only thing I wanted to say on that.

Senator KENNEDY. Who decided that?

Mr. MOYLE. I think it was a joint decision of Dr. Jacob and Dr. Pani.

Senator KENNEDY. Did you leave a copy of the Scherbel report with Dr. Pani, or did you just show it to him? Do you remember?

Mr. MOYLE. I know we showed it to him, Senator. My recollection is not firm on whether we left him a copy or whether he said, "It is not that important." I just do not remember.

Senator KENNEDY. But your testimony is that you brought these potential side effects to the attention of Dr. Pani in person?

Mr. MOYLE. Yes, sir.

Senator KENNEDY. And you have heard him state that you did not, and you stand by your testimony?

Mr. MOYLE. I heard most of his statement today, yes, sir.

Senator KENNEDY. You, in fact, wrote Scherbel on May 17, 1977, telling him that you showed it to Dr. Pani, did you not?

Mr. MOYLE. Yes, sir.

Senator KENNEDY. But in your cover letter to Dr. Merle Gibson at the FDA, where you state that you are enclosing Dr. Scherbel's work, you do not flag the significance of the progress report and point out that eye toxicity is mentioned by Dr. Scherbel.

Mr. MOYLE. I did not think that it was; I did not see that there was eye toxicity.

Senator KENNEDY. Pardon?

Mr. MOYLE. I am not a doctor to evaluate that, but my understanding was that there was no high toxicity mentioned.

Senator KENNEDY. Well, you still wrote to Dr. Scherbel to ask him for additional information, did you not?

Mr. MOYLE. I wrote to Dr. Scherbel; I think I have a copy of the letter.

Senator KENNEDY. Yes; you said you were most anxious to see how these cases were progressing in his next report.

Mr. MOYLE. Yes.

Senator KENNEDY. So you thought that they were of some importance at that time.

Mr. MOYLE. We tried to follow everything up as well as we could.

Senator KENNEDY. But you did not flag it in your later letter, though, did you, to FDA?

Mr. MOYLE. I am sorry; I am not sure which letter you are——

Senator KENNEDY. Well, in fact, you wrote to Dr. Scherbel on May 17 telling him that you showed it to Dr. Pani, did you not?

Mr. MOYLE. Yes, that is correct.

Senator KENNEDY. But in the cover letter to Dr. Merle Gibson at the FDA—that is the letter I am talking about here, where you state that you are enclosing Dr. Scherbel's work—you did not really mention at that time the significance of the progress report and point out the eye toxicity mentioned by Scherbel.

Mr. MOYLE. I think it says we enclosed the reports themselves. I am not sure it would be my position to judge that.

Senator KENNEDY. Do you mention that in your cover letter?

Mr. MOYLE. I mention that it is a report on IND 13097, which was the oral scleroderma IND.

Senator KENNEDY. But in the cover letter, do you mention anything about eye toxicity?

Mr. MOYLE. Well, I was not in a position to formulate an opinion as to that letter of Dr. Scherbel's. I simply wrote a letter of transmittal for the letter, as we normally did, as a routine matter.

Senator, I might just say that I do not think that any one of my associates took that letter as a serious toxicity problem. It may be that perhaps I made a mistake; I do not know.

Senator KENNEDY. The point is that the enclosure is not in the FDA file. They did not get the cover letter either, and the other letter is not included in the FDA file, so there is nothing in the FDA file.

Mr. MOYLE. My records would indicate that this was what was included with the letter to the FDA on those patients.

Senator KENNEDY. Well, of course, the FDA says they have none of it. You said that it is a question of fact. We cannot resolve it here.

Mr. MOYLE. That is correct, Senator.

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Senator KENNEDY. It is a matter of enormous importance and consequence, and it is going to have to be a matter that is going to be judged, or at least evaluated, by the Justice Department, because we certainly cannot do it.

But, obviously, I want to give you the chance to state what you did and the steps that you took and the actions that you have taken.

Mr. MOYLE. Well, of course, I felt at that time that calling it to Dr. Pani's attention was adequate. Nobody was really concerned about it.

Senator KENNEDY. In September 1979, Dr. Scherbel, in another letter to you, mentioned additional patients who had received either oral or parental DMSO, who had had cataracts. Was this information ever passed on to the FDA for evaluation?

Mr. MOYLE. I do not have that information with me, Senator. I could look it up.

Senator KENNEDY. Excuse me?

Mr. MOYLE. I am sorry; I do not have that information, and I do not have a recollection.

Senator KENNEDY. As I understand it, in the September 7, 1978, progress report to FDA you state, "To date, our investigators have reported no abnormalities relating to the toxicity of the drug, nor have they reported any ocular abnormalities."

Mr. MOYLE. That is correct.

Senator KENNEDY. Here, you highlight the absence of ocular abnormalities in your transmittal letter, but you never highlighted any potential problems.

Mr. MOYLE. That was, in fact, true; there was no DMSO-related toxicity.

Senator KENNEDY. Well, let me just see if I understand what I see as the significance here. People have been concerned about whether DMSO might cause eye damage in humans. The first indication that this might be so was contained in a study done for your firm.

That study never made it to the FDA files. You claim you delivered it; you do not recall whether you ever mailed it in officially. Dr. Pani claims it never came and the fact is that FDA was in the dark about it until this year. You have heard the Commissioner of the FDA say that it is as serious a violation to the act as he can imagine.

In addition, we have seen, in another instance where DMSO is actually approved for marketing, that one of the studies upon which that approval was based is worthless, and another is in question. And yet, this is a drug that hundreds of thousands of people are using, and for which there is great public pressure and for which there is great congressional pressure.

Now, that record itself is enormously distressing and disturbing, and it is a potentially dangerous record. Compounding this is the failure of the FDA to properly handle this drug, failure to give it an efficient and effective review, and failure to move expeditiously when problems are discovered. The result is that a travesty has been made on the regulatory process and serious questions have to be in the minds of hundreds of thousands of Americans who need

and want to use a drug that may alleviate their suffering from a variety of ailments.

It seems to me that the people are entitled to better performance; they certainly are entitled to better performance from the FDA. It seems to me that they would be entitled to a better performance by the private sector as well. In the interest of the people who are suffering and are full of anguish and anxiety, it seems to me that we ought to be able to get a quick, accurate, and definitive answer to those Americans.

I do not know whether you have any reaction.

Mr. MOYLE. Senator, I could not agree with you more. We have spent our last 8 years and spending almost my full time trying to do that. We have done the best job we know how; I am certain it is not perfect, but I am certain it is substantially accurate. I think there is no question but that we can prove that.

We have never seen the data that has been generated by investigators in this case, and perhaps if we could see it and get together with them, we could figure it out. But we have never had that opportunity, and we would like to have it so that the American people can be advised as to the status of the drug now and what we are doing in the future.

We have hired three doctor monitors and two nurse monitors to properly monitor everything we are doing at the present time. The FDA is cooperating with us like they never have before, and we appreciate that.

Senator KENNEDY. Well, you do have a responsibility in monitoring that material, do you not? You certainly have some responsibility for monitoring that material and making sure that it is accurate.

Mr. MOYLE. I understand our monitoring much better now than I ever did before.

Senator KENNEDY. Yes. Well, the problem is whether people have been put in jeopardy because of that. This is something that we cannot say with any definite assurance, but it seems to me that there is that responsibility within the company. Besides the responsibility of FDA, there is certainly that responsibility by your company as well.

Mr. MOYLE. Well, we have certainly accepted that responsibility and, within our means, we are doing everything I know we can do, and we will accept suggestions from anyone here or at the FDA as to how we can improve further.

Senator KENNEDY. Dr. Jacob, I know you have spent many years and a great many hours working with a drug that you believe to be of significant benefit to the American people. I want to assure you that the interests of the committee and your own interests are the same, and that is to get the promptest possible, definitive evaluation after all this time, so that the American people will know whether or not DMSO meets the standards that every other pharmaceutical product is required to meet.

To the extent that the rigid bureaucracy has been holding up the approval of the drug, this committee would try and cut through that. I think we have some assurances from the Commissioner on this now, and we will follow up, because we intend to stay after this situation.

To the extent that the scientific questions are holding up the drug, the committee will seek to assure that those questions are answered properly and in a sound scientific manner.

In my opinion, the bureaucracy has been at fault here, but so has the quality of the science that has been done in the study of this drug. One of the problems FDA now confronts is the fact that the Shirley study of DMSO for use in treatment of disease is now considered unacceptable by that agency.

You were the monitor of that study. How would you assess your own performance as the monitor for Research Industries?

Dr. JACOB. Senator Kennedy, I think that perhaps I should have made more visits to some of the centers where DMSO studies were being conducted. But I did see the investigators in Washington; I talked to them frequently by phone.

I think a little bit of background here would set the record straight. It has been made to look by FDA people this morning that this is a noninvestigated drug or a poorly investigated drug. It is the most thoroughly investigated experimental drug in the history of medicine.

Senator KENNEDY. Now, that is quite a statement.

Dr. JACOB. I am willing to make that statement and stand on it, sir.

Senator KENNEDY. You will submit the studies or give references?

Dr. JACOB. I have it in my statement.

Senator KENNEDY. You are saying that this is the most studied drug in the history of medicine?

Dr. JACOB. Yes, sir.

Senator KENNEDY. Why do you not continue? Do you have a list of the studies?

Dr. JACOB. In my statement, I mention seven technical books. In our bibliographic reference file at the medical school, we have 3,800 references from around the world which we have studied. There is no evidence for ocular toxicity in man. We have carefully done studies on prisoner volunteers. I personally was associated with these in 1968 at the Vacaville Medical Facility.

In 1964–1965, Merck, Syntex, Squibb, Geigy, Shearing, and American Home Products submitted data on 100,000 patients to the FDA receiving DMSO. The FDA at that point turned down three NDAs—one from Merck, one from Syntex, and one from Squibb. They turned down a fourth NDA from Squibb in 1970.

Senator KENNEDY. You made the statement about the most extensive study that has ever been made with regard to a drug.

Dr. JACOB. Yes, sir, and I stand on that.

Senator KENNEDY. Now, we have the two studies upon which this was approved, on which the FDA has done a reexamination and has found those studies to be faulty on the basis of scientific information, including the alteration of data and the change of documentation on those studies. Those were the studies upon which this drug was approved.

Now, that is the testimony of the FDA. We are not scientists up here. We are not talking about the numbers; we are not talking about antidotal kinds of information. We are talking about hard scientific information.

They have stated that the two studies that were submitted for the approval of that drug were faulty. That is their sworn testimony.

Now, I am not interested in how many textbooks have been written about it. We are generalists; we cannot make a judgment on all of the textbooks; that is not our responsibility.

What we do hear is what the FDA has stated on this, and we are not here to say whether there have been misunderstandings on these studies, or what the facts are. We do know that there is a direct conflict in sworn testimony here about some very basic and fundamental scientific information. That is going to the Justice Department.

Dr. JACOB. Yes, sir.

Senator KENNEDY. For you to come on up and just sort of state that this is the most studied drug and we have umpteen books that have been written about the subject matter does not meet the principal statement or charge that the FDA has made, and that is that the Stewart and Shirley studies were basically faulty from a scientific point of view.

Dr. JACOB. I do not agree with that, Senator Kennedy.

Senator KENNEDY. Pardon?

Dr. JACOB. I do not agree with the FDA's appraisal of that.

Senator KENNEDY. Well, you do not agree, but they have investigators and they have done that review. You might not agree, but they have at least made those judgments and have outlined the reasons for them. They have talked about changed information; they have talked about faulty scientific information, and they have made that judgment. That is something that you do not agree with, but nonetheless they have made that charge.

We are interested, obviously, in listening to your comments, but I do think that you have listened to their testimony here and you are obviously welcome to make whatever comments you want.

Dr. JACOB. I would like to, Senator Kennedy. In 1965 when Merck, Syntex, and Squibb submitted new drug applications to the FDA, in the spring of 1965, stating that DMSO was safe and effective, as I say, there were data on over 100,000 patients submitted to the FDA.

The FDA halted studies in November of 1965 on the basis of "blue-sky" testing and the question of ocular toxicity in lower animals, particularly the rabbit. Two weeks after they halted studies, they called inspectors from the 12 major districts in the United States to Washington and they said, in essence, "we are not sure of ourselves; this is probably a safe drug and it is probably an effective drug; go out and justify what we did and find us some pigeons."

Following that, they launched into the most vigorous investigation that had ever been done by the FDA up to that point. It was so vigorous that they had to call in the FBI because there were some 1,500 physician investigators in the United States.

Subsequent to that, very careful studies I helped work with, sponsored by Squibb, showed there was no ocular toxicity in man. Very careful studies in lower primates, where monkeys were given 3 grams per kilogram orally for 18 months, show that there is no ocular toxicity in lower primates.

I have visited every country where DMSO is prescriptive. I have talked to regulatory authorities. I have studied every paper that I can get my hands on. There is no evidence for ocular toxicity in man with this compound, Senator Kennedy, and I think the FDA knows it.

I believe a pseudoscientific game is being played with the American people. This is an inexpensive compound which is not patentable, I think there are other reasons for its blockade besides what was mentioned this morning.

Senator KENNEDY. What could possibly be the purpose of the FDA to try and deny suffering American people the opportunity of relief from pain? What would possibly be their purpose or their motivation in trying to do that?

There are standards which have been established which other drugs in our society have to meet, in order to try and establish the safety and efficacy for protection of the American people.

Now, they have made the judgment on the basis of the reports that have been submitted by the company itself that the studies are indeed faulty, and they have found other problems. You say that those problems are nonexistent. We are not in a position to say whether they are or they are not. We are not scientists; that is not our function.

Our function is to try and insure that the FDA is going to work effectively so that new drugs will be available to relieve the pain and anguish of people, and also to insure that people are going to be protected. We have an oversight responsibility, and that monitoring system which has been described here is the direct result of actions that has come out of this committee as a result of a series of abuses that we have seen in industry a number of years ago. So, we are familiar with that monitoring system.

Now, why the agency would make allegations and representations that factual misstatements and alterations of data had been made, in order to deny the American people the kind of relief that we heard of from the first panel of witnesses is something that I would not be able to understand or comprehend.

You believe that they have.

Dr. JACOB. Yes, sir, I do.

Senator KENNEDY. You believe that very strongly.

Dr. JACOB. Yes, sir.

Senator KENNEDY. But the fact of the matter is that they are scientists and they are researchers, and they have profound responsibilities. I am sure that they have, with all due respect, as much interest in seeing the American people relieved of anguish and anxiety and pain as anyone else; no one has a lock on that particular virtue.

It seems to me that what we have seen that over a score of years is there has been a bureaucracy, a failure of monitoring, a failure of oversight, and a failure of science in this area.

The principal concern that I have and that the committee has is what the American people are going to think about this when they see an agency of Government that has a responsibility for being able to do an evaluation of scientific information and monitoring makes one judgment, and a doctor who is the principal proponent

of this particular drug, and has a financial interest in it, takes strong exception with that judgement.

Now, we have recommended that we convene a meeting and establish a process and procedure by which we get the definitive answers. I outlined that in my opening statement and comments. We can get the Commissioner, the NIH, and the FDA. We have invited the company and they have indicated a positive response. And we would welcome your involvement as well, to at least establish and set up a process and procedure where we are going to get that information and make some final, determinant judgments on these matters so that the American people can at least be able to know, finally, the answers to the questions which have been raised and which must be raised in the minds of people, even as they watch these hearings today.

I just have a final question. Do you remember being with Mr. Moyle at the time that information was given to Dr. Pani?

Dr. JACOB. Yes, sir.

Senator KENNEDY. And do you know whether you left that information with him?

Dr. JACOB. I do not believe we left it at that point.

Senator KENNEDY. You just showed it to him?

Dr. JACOB. We just showed it to him.

Senator KENNEDY. Well, we will set up the time of the meeting and we will look forward to having your participation. Thank you very much.

[The prepared statement of Dr. Jacob and additional material supplied for the record follow:]

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UNIVERSITY OF OREGON
HEALTH SCIENCES CENTER

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Sub-Committee on Health
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The passage of the Kefauver-Harris amendments in 1962 has been followed by an obvious drug lag in the United State. By "drug lag" I mean:

1. Reduced rate of discovery and development of new therapeutic entities.

2. Increased period of time to move new drug discoveries from the laboratory to prescriptive use.

3. Restricted release of new drug entities in the United States compared with other technically advanced countries.

Since 1962, the United States Food and Drug Administration has grown in both power and population -- in many ways like a malignant tumor. There are at least four serious side effects secondary to the way the FDA has functioned:

1. FDA regulations have increased the cost for therapeutic substances.

2. FDA regulations have brought about a termination of research on many therapeutants which might be useful in so-called "orphan" diseases, i.e., diseases affecting fewer than 100,000 Americans.

3. FDA regulations have brought about a de-emphasis of research and development of the so-called "soft" (less toxic) drugs which are difficult or impossible to clear through the present methodology of efficacy required by the FDA. If aspirin were to be introduced today, it would fall into the category of a "soft" agent of low toxicity.

4. The FDA has brought about a de-emphasis of research and development on drug combinations.

I would like to discuss dimethyl sulfoxide (DMSO).

My major research interest since 1962 has been the pharmacology and clinical usefulness of DMSO.

Dimethyl sulfoxide in the United States is derived from lignin, the cement substance of trees. It can, however, be made from a number of organic chemicals and may be inexpensively produced.

DMSO was first chemically prepared in 1866 but remained a laboratory curiosity for more than three quarters of a century. In 1948, a number of papers began to appear in the chemical literature showing it was a solvent for many other substances. In 1959, a group in Great Britain demonstrated that dimethyl sulfoxide would protect red blood cells and other tissues against freezing damage.

The use of DMSO as a drug was not shown until a collaborative effort between scientists at the University of Oregon Medical School and the Crown Zellerbach Corp. demonstrated in laboratory tests that DMSO would not only pass through the skin and mucous membranes, but during passage would carry with it a certain number of other substances. For instance, Penicillin can be dissolved in DMSO and be carried through the skin without a needle.

In these early studies, dimethyl sulfoxide was shown to relieve pain, reduce swelling, slow the growth of bacteria, improve blood supply, soften scar tissue, enhance the effectiveness of other pharmacologic agents, serve as a diuretic, and act as a muscle relaxant.

The first report on the use of dimethyl sulfoxide as a pharmacologic agent was written in 1963 and published February 1, 1964. The first IND to study DMSO clinically in the United States was submitted on October 25, 1963. Three NDA's on DMSO were submitted to the FDA in 1965. All were turned down. A fourth NDA was submitted in 1970. It was also turned down by the FDA.

Yet, the New York Times in a lead editorial on April 3, 1965, called DMSO "the closest thing to a wonder drug produced in the 1960's."

Several thousand scientific articles on DMSO have appeared in the world's literature. In our reference library at the University of Oregon Health Sciences Center, we have a fairly complete bibliography which includes seven technical books on dimethyl sulfoxide.

Four international symposia have been held on DMSO. The first of these was in Berlin, Germany, in July, 1965. The second was under the auspices of the New York Academy of Sciences in March of 1966, New York City, New York. The third was sponsored by the University of Vienna, in Austria, November, 1966. The fourth was again in New York, under the sponsorship of the New York Academy of Sciences in January, 1974.

Of major importance is the fact that DMSO has been shown to be of value, not only in diseases for which there is other known treatment, but in a number of illnesses for which no other effective or low risk treatment is known, such as the painful ulcers of the fingers in patients with scleroderma. In this disease the skin becomes tight and the joints are prevented from moving.

Microscopic sections of skin from patients with scleroderma have been studied before and after treatment of DMSO. These studies demonstrated definite improvement with DMSO therapy--without DMSO, some of these patients would require amputations.

The value of DMSO in other illnesses for which effective pharmacologic treatment does not presently exist, includes severe abacterial prostatitis, Dupuytren's contracture, subcutaneous scarring from cobalt irradiation, keloids, Peyronie's disease and potentially in otherwise "irreversible" injury to the brain and spinal cord.

A broader spectrum of primary pharmacology and clinical benefit, both actual and potential, has been described in the scientific literature for DMSO than for any other substance with which I am familiar. No attempt will be made at this point to record the long list of entities for which benefit from DMSO has already been responsibly reported in the literature. In my opinion, DMSO is the treatment of choice for severe acute musculoskeletal trauma (such as strains and sprains) and acute and chronic bursitis.

Dimethyl sulfoxide is a useful adjunct in the treatment of rheumatoid arthritis, degenerative arthritis and gouty arthritis. It primarily will relieve pain, but will also reduce inflammation and increase joint mobility. Due to its effectiveness in the treatment of arthritis, Americans by the thousands are flocking to nations such as Mexico to receive DMSO. In Mexico they are charged seven to eight hundred dollars for three days of treatment. One entrepreneur in this "South of the Border" country presumably treated with DMSO thirty-thousand Americans last year for arthritis and grossed over twenty million dollars.

The effectiveness of DMSO has been demonstrated by comparative studies, by "double blind" studies, and by the clinical impression type of evaluations in man.

Dr. J. Harold Brown, formerly President of the Aerospace Medical Association, included in this "double blind" report the following statement:

> "I am convinced that topical application of DMSO in the treatment of acute musculoskeletal conditions is a striking and significant therapeutic contribution. During the period of time I conducted clinical investigation with this medication, I practically discarded physical therapy as treatment for musculoskeletal problems because the rehabilitation of my patients was so prompt with DMSO. There was little or no necessity to prescribe narcotics and tranquilizers since pain was promptly mitigated following topical application of DMSO."

The further usefulness of DMSO has been shown by the fact that it is now prescriptive in the United States for acute musculoskeletal problems in small and large animals, approved by the Veterinary Division of the Food and Drug Administration in 1970.

An important question about any drug is toxicity. There is no such thing as a non-toxic drug. DMSO has its side effects. The major side effect of DMSO is the possibility of an occasional patient being hyper-sensitive.

I believe there are more data on animal toxicology regarding DMSO than have ever existed for any other experimental drug. I have not had experience with any drug in medicine which I consider to be safer. In my estimation there are more data on human toxicology of DMSO than have ever been obtained for any other experimental drug. The Food and Drug Administration itself has data on over one hundred thousand patients. Despite the prescriptive use of DMSO world wide, there is, to my knowledge, not a single case of well-documented serious toxicity.

Dimethy sulfoxide is currently a prescriptive agent in the United States for interstitial cystitis. It is prescriptive in Canada for scleroderma. It is prescriptive in Great Britain and Ireland for shingles when mixed with IDU. It is prescriptive for a whole range of disorders for topical administration in Germany, Austria, and Switzerland. It is widely prescriptive in many parts of South America. It is prescriptive in the Soviet Union and has been since 1971.

When Dr. Chauncy Leake, one of the world's most eminent pharmacologists, reviewed the New York Academy of Sciences Symposium on DMSO in 1966, he stated that the well known legal phrase "res ipsa loquitur" applied to the DMSO situation. In summarizing the conference, Dr. Leake said,

> "Rarely had a new drug come to the attention of the scientific community with so much verifiable information, from so many parts of the world, both as to safety and effectiveness."

There is little doubt but that DMSO should be prescriptive in the United States today for a whole host of disorders, including its potential for pain relief in arthritis. It is prescriptive only for one numerically insignificant entity, interstitial cystitis.

I am willing to make the statement to this Committee that there is no question concerning the effectiveness of DMSO. It is one of the few agents in which effectiveness can be demonstrated before the eyes of the observers. For instance, if we have patients appear before the Committee with edematous sprained ankles, the application of DMSO would be followed by objective diminution of swelling within an hour. No other therapeutic modality will do this.

If we have patients appear with acute bursitis unable to move a shoulder in any direction, the topical application of DMSO would be followed by a dramatic increase in the range of motion at the end of a half hour. If we have patients appear with chronic bursitis, the topical application of DMSO would be followed by a notable increase in the range of motion within a half hour.

If we have patients appear with fresh ecchymoses such as an early black eye, a topical application of DMSO would be followed by a reduction in this discoloration within one hour.

An NDA on DMSO for scleroderma was submitted almost three years ago. During this time we have revised the submission several times to meet decision delaying tactics. This NDA was turned down by the FDA. The FDA is currently considering whether to require additional months, or most probably years, before they approve this indication. These delays cause unnecessary suffering for thousands of Americans and possibly the loss by otherwise unnecessary amputation of fingers, toes, and limbs. This is an intolerable situation.

Dimethyl sulfoxide (DMSO) is a particularly promising treatment with injuries of the central nervous system (brain and spinal cord). Data from lower animals and man indicate that DMSO may be more important than any other pharmacologic agent in treating injuries to the brain and spinal cord.

With such a promising new medical application for DMSO, one might presume that we are satisfied and optimistic about the project's future. This is far from the truth. Results with CNS accidents, to date, though dramatic and life-saving, are not even fractionally different from multiple clinical findings with DMSO for other disorders.

Heretofore, every time we have concluded a clinical study demonstrating efficacy and safety with DMSO, we have been rewarded with a new stabilized, FDA position of confoundment. An obdurant barrier of bureaucrats housed in the offices of the FDA has shredded the data with their own, unique methodology. In their house, supported by public funds, they play dangerous games--harmful games with truth, statistics, objectivity, ethics and the health and welfare of citizens of the U. S. If their policies with DMSO are an accurate barometer of their general procedures with food and drug policies, the Bureau, itself, may be a great hazard to the health of the people of this country.

Let me make a grim prediction concerning the fate of our CNS-DMSO projects. Unless responsibility for DMSO decisions are removed from the FDA or the FDA is subject to a radical change in management, despite the potential savings of tens of thousands of lives per year or prevention of permanent paralysis, post-CNS accident, FDA will continue to block public access to the drug for at least several years. Recall the so-called "historical" control to this matter--FDA has blocked other important medical usage of DMSO in man for more than 15 years.

The major question continues to be, has the public benefited, or has the public been harmed by the FDA blockade on approving DMSO. If DMSO has been truly a nostrum, or even worse, a drug associated with serious clinical toxicity, the public would have benefited by FDA actions. If, as overwhelming scientific evidence indicates, DMSO is a significant medical advance with minimal clinical toxicity, then the public has been and continues to be harmed by the FDA approach.

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Associate Professor
Department of Surgery

TESTIMONY SUBMITTED BY SENATOR JAMES McCLURE AND CONGRESSMAN STEVEN SYMMS ON DMSO, DIMETHYL SULFOXIDE, JULY 31, 1980.

Mr. Chairman and Members of the Committee it is a privilege for Senator McClure and me to submit testimony today on the innovation and availability of DMSO in the United States. Furthermore, we would both like to commend the Committee for making an effort to investigate the uses of this compound.

As you know, both Senator McClure and I have introduced three bills in the Senate and House, respectively, which would approve the usage of dimethyl sulfoxide for the treatment of scleroderma, arthritis, bursitus and other muscular skeletal disorders and approve the intravenous use of DMSO for the treatment of acute brain and spinal cord injuries. In addition, we have both cosponsored legislation which would direct that a clinical investigation of the safety and efficacy of DMSO as a drug to be used by persons with arthritis be conducted through the NIH National Institute of Arthritis, Metabolism and Digestive Diseases.

Under normal circumstances, neither of us would introduce legislation for the specific approval of drugs because a) as a general policy it is not wise for non-medical individuals to approve or disapprove of the use of specific compounds and, b) we believe that the entire process by which the Food and Drug Administration approves drugs for use in the United States should be revamped. In this regard I, Congressman Symms, have introduced a major drug reform bill, H.R. 54, the Food and Drug Reform Act of 1979.

However, because DMSO can provide widespread relief for those suffering from muscular skeletal disorders such as arthritis; provide treatment to those suffering from scleroderma, a disabling disorder in which the skin becomes tight, interfering with blood

supply and joint movement; and often times save the lives of those patients who are suffering from injuries or hemorrhaging within the brain because of its abilities to reduce intracranial pressure, we believed that specific legislation was urgently needed to make DMSO available for prescriptive use in the United States.

Despite a myriad of tests and a multitude of patients attesting to the safety and efficacy of DMSO, the Food and Drug Administration still enforces its "go-slow" edict on DMSO. On April 20, 1980, in a meeting I, Congressman Symms, had with Dr. Stanley Jacob of the University of Oregon Health Sciences Center, Dr. Stark of FDA, Dr. Marianne Finkel of FDA, and Mr. Larry Gage of the HHS Congressional Liaison office, the officials from FDA stated that DMSO was safe for use but that they could not approve of its use, except in the treatment of interstitial cystitus, because it did not meet their efficacy standards in a controlled lab experiment. The efficaciousness of the drug has been difficult to prove in the lab because it cannot meet the standards of the "double-blind" test due to the garlic or oyster-like taste that occurs when the drug is applied topically, and because DMSO has a systemic effect -- it enters the blood stream upon application and as a result it will not only treat the area to which it was applied but it treats other areas of the body as well.

In a recent HHS Press Release, Dr. Goyan maintained that it is not safe for individuals to use DMSO without any medical supervision. Both Senator McClure and I would totally agree with Dr. Goyan on this matter and that is exactly the reason why the drug should be approved for prescriptive use in the United States. Furthermore, Dr. Goyan stated that the FDA is anxious to have tests completed

on the efficacy of DMSO. However, while we encourage and support further testing of DMSO to prove its efficaciousness in controlled lab experiments, the fact remains that it will take several years before those experiments are completed. During that time period, numerous scleroderma patients will have to have their fingers and toes amputated, numerous arthritic patients will suffer needlessly and numerous patients will become quadraplegics all because DMSO, which is safe for use, has not been proven effective, according to FDA standards, in the lab.

There is very little that can be said in a complimentary vein for the FDA for it has been a tremendous obstacle to the progress of medicine. The FDA has been solely responsible for driving modern medical research out of this country to foreign soil. Unfortunately, the attitude that more regulations and prohibitions will insure the safety of the citizens of the United States is totally distorted. The fact of the matter remains that FDA constraints have caused undue suffering and the loss of life and limb to many of the citizens here in the United States. DMSO is an example of but one drug that the FDA has withheld from the American market which could possibly treat or cure those afflicted with an illness.

It is our hope that by this Committee holding these hearings on DMSO, the Food and Drug Administration will not only release this drug for prescriptive use more quickly, but that the FDA will also realize that the Congress and citizenry are calling for substantial reform of the drug approval procedure.

Again, thank you for the opportunity to make our views known on DMSO and the need for drug reform.

Senator KENNEDY. The committee is in recess.
[Whereupon, at 12:15 p.m., the subcommittee was adjourned.]

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